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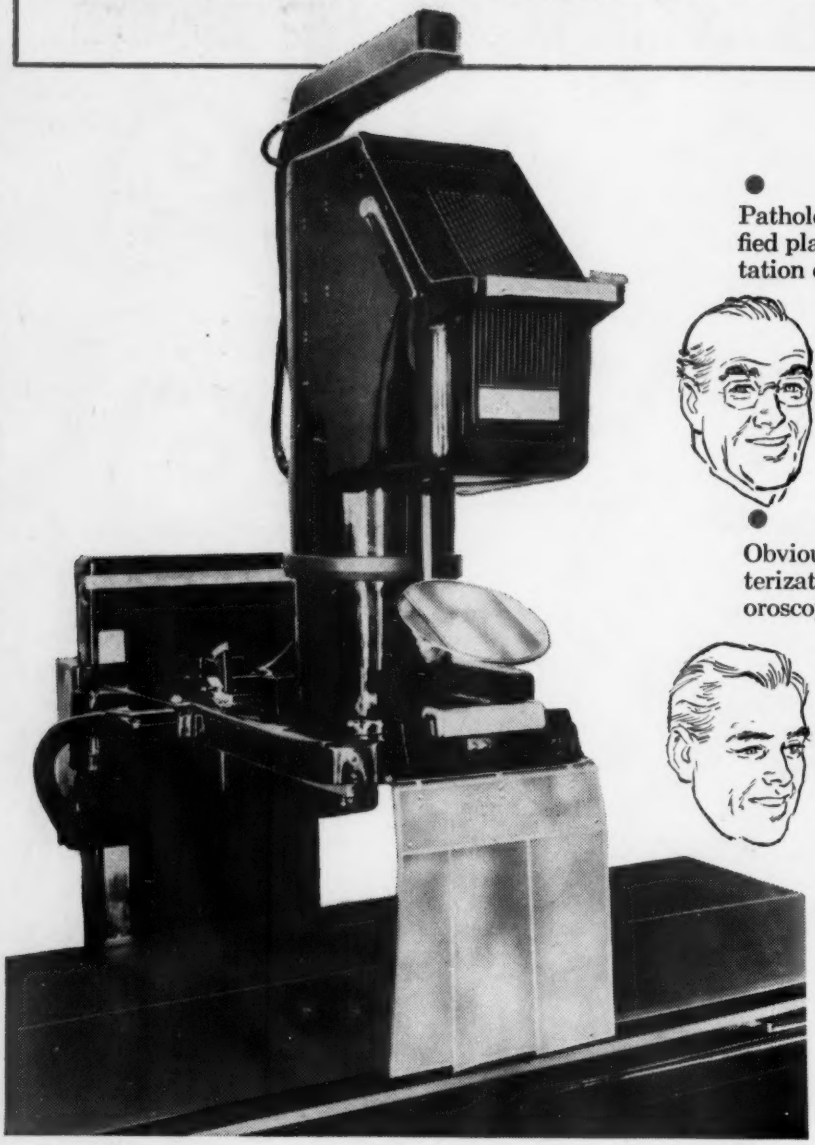

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THE AMERICAN JOURNAL OF ROENTGENOLOGY
RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 74 OCTOBER, 1955 No. 4

THE ROENTGEN SIGNS OF GASTRITIS*

CLINICAL ANALYSIS

By L. WALK, M.D.
ESKILSTUNA, SWEDEN

IN A previous paper, in this journal,[27e] I have summarized my work on the roentgen signs of gastritis. In the following, an analysis of the mucosal folds in gastritis is reported, and the roentgen signs are analyzed together with clinical findings by which method more information is gained than if roentgenograms alone are used.

MATERIAL AND METHOD

The material comprises 252 cases, with the roentgen findings controlled by gastroscopy. In 7 there was a gastroenterostomy, and in 30 a gastric stump after partial resection. In 41 cases, even a histopathologic examination of the resection specimen of the stomach and in 1 of a biopsy has been performed.

The roentgen examination is started in recumbent position, to bring the barium in contact with the fornix, after which the patient is turned to the prone position. Roentgenoscopy is immediately continued standing. The barium is distributed in the stomach by palpation and, if possible without delay, the duodenal bulb is filled. A survey film, usually one to two minutes after the intake of the barium, and compression films for relief study are made. In the remaining, the technique is the same as in ordinary gastric exploration.

A. *Gastric Configuration.* The separation of a shorter, hook-formed stomach from a longer, vertical one (Fig. 1) has been subjective. A gastric index[11,14a] would have made the roentgen signs too complicated to be used in current work.

In catarrhal gastritis, with reddening as well as swelling, a hook-formed stomach is more frequent than in normal mucosa (Table 1). In the table, the ordinary numbers are the total number of cases, whereas those in parenthesis are cases with no other gastroduodenal disease (except for small polyps or mucosal erosions) which might modify the roentgen findings. In mucosal atrophy, in the uncomplicated cases, a hook-formed stomach is about as frequent as in normal; if the total number of cases of atrophy is compared to normal, however, a hook-formed stomach is more frequent.

* From the Roentgen Department and the Department of Surgery, Central Hospital, Eskilstuna, Sweden.

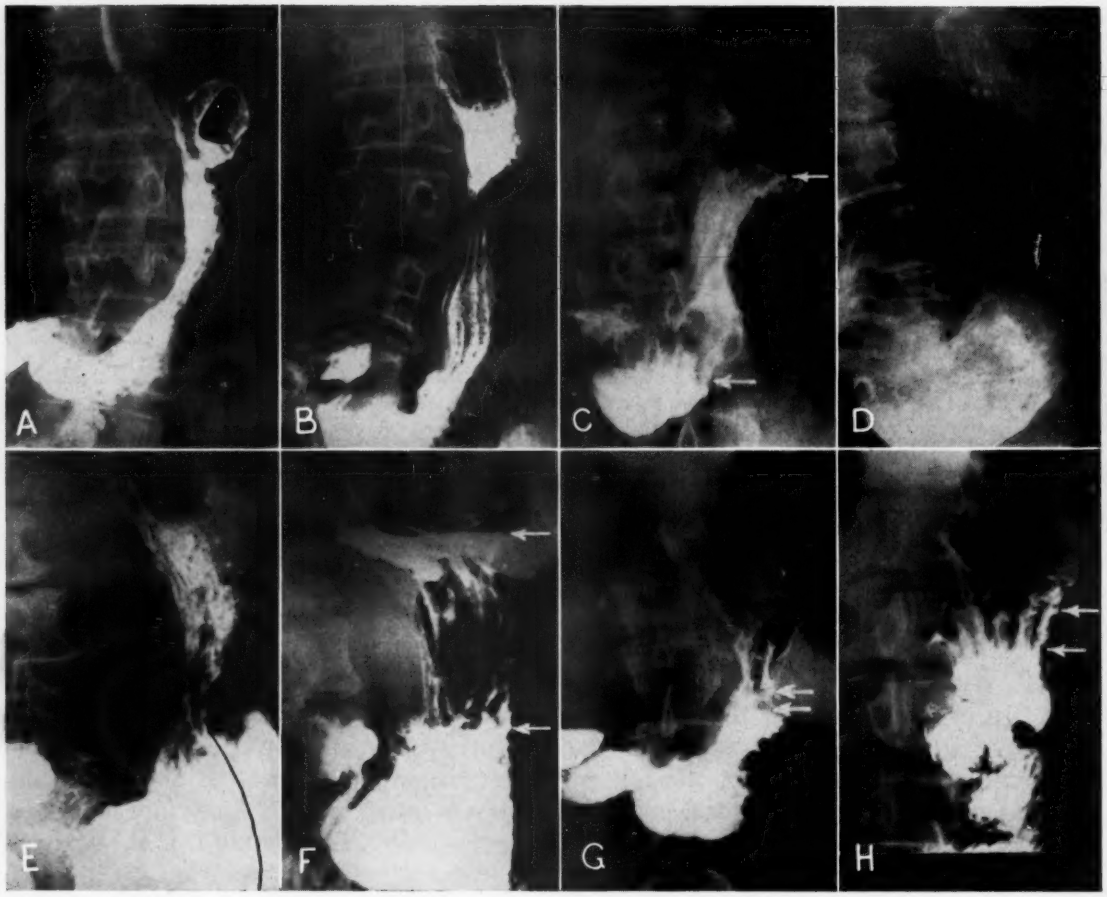

Fig. 1. Gastric configuration, intermediary fluid and secretion (description in text). (*A*) Hook-formed "dry stomach." (*B*) Vertical "dry stomach" (see Fig. 2*A*). (*C*) Hook-formed stomach with medium-sized intermediary fluid (arrows) (see Fig. 2, *B* and *C*). (*D*) Good mixture of barium with intermediary fluid in mucosal atrophy and stenosing prepyloric tumor, (*E*) same case after partial evacuation of the ectatic stomach before the roentgen examination. (*F*) Hypersecretion, sharply demarcating layer (arrows) not easily mixed with barium by palpation. (*G*) Short, hook-formed stomach with minimal intermediary fluid (arrows). (*H*) Intermediary fluid in gastric stump in catarrhal gastritis with swelling (see Fig. 2*H*).

On the contrary, in cobblestone mucosa, a vertical stomach is slightly more frequent than in normal. As far as I know, this has not been mentioned in the literature. Differences in the roentgenologic appearance, however, have been reported without gastroscopic controls;[11] although with a technique different from that used by me (the stomach has been *filled* with barium, whereas in our material small quantities were given to outline the relief, and the appearance was recorded before continuing the examination), the findings are in agreement with our material.

B. *Mucosal Folds.* In the previous article, I have used a simple description of the mucosal folds (thin, ordinary, and thickened). This did not render any definite possible conclusions, and in the following the folds have therefore been measured.

The method of measurement is important, which apparently is not known in the literature. A compression, just sufficient to demonstrate the folds, has to be used. High compression would cause artefacts, as the folds are flattened and therefore appear much thicker than in reality (Fig. 2*A*). If

TABLE I

ROENTGENOLOGIC CONFIGURATION OF THE STOMACH IN GASTRITIS. ANALYSIS OF 213 CASES. NUMBERS IN PARENTHESIS ARE CASES WITH NO OTHER GASTRODUODENAL DISEASE

Gastroscopic Findings	Number of Cases	Gastric Configuration			
		Diagonal	Hook-formed	Vertical	Long vertical
Mucosal atrophy, pronounced	19	—(—)	13 (8)	4 (3)	2* (—)
Mucosal atrophy, slight	14	1 (1)	9 (8)	4 (2)	—(—)
Normal mucosa	76	1 (—)	37 (22)	34 (8)	4 (2)
Catarrhal gastritis, reddening	52	1 (—)	32 (23)	17 (5)	2 (—)
Catarrhal gastritis, swelling	21	1 (—)	13 (6)	5 (1)	2 (—)
Cobblestone mucosa	31	—(—)	11 (2)	19 (4)	1 (—)

* Two cases of ectatic stomach in stenosing tumor.

this is not carefully kept in mind, very confusing errors will arise, *e.g.*, folds of 4–4.5 mm. may be recorded as 6–6.5 mm. and more. To avoid differences by projection, the distance of the film to the patient was kept constant; a conception of the size of the folds, however, was frequently obtained from films of different roentgen institutions. Instead of a cone, a small oval pillow was placed between screen and patient, to enable compression out of the center of the picture if necessary, and to push the barium upward in a stomach with intermediary fluid. By this method, the folds may even be visualized in an ectatic stomach, provided that they are not flattened by the distention due to the gastric contents. The folds are thinnest at the lesser and thickest at the greater curvature. They have been measured in the lower corpus or in the sinus, at some distance from the curvatures. Uniform compression is obtained in a small area only. Roentgenograms showing the folds, coated with barium, against air in the stomach (with the patient in recumbent position) could also be used. In prone position, the folds appear thicker because of a greater stomach-film distance, and cannot be measured. An idea was frequently obtained on survey films, with the patient standing, provided that there was no considerable fluid.

C. *Intermediary Fluid and Secretion.* The intermediary fluid is seen on a film with the patient standing (Fig. 1, Table III). In our material, there is a definite parallel of what is observed roentgenologically and of the amount of fluid removed from the fasting stomach before gastroscopy in a moderate Trendelenburg position. The estimation of the secretion, however, is subjective. Rapid accumulation of secretion, with a sharply demarcated layer not easily mixed with the barium, has been recorded as hypersecretion. If roentgenoscopy is performed rapidly, the secretion appears to be less than in prolonged examination where palpation is interrupted by long pauses. Where a high position of the stomach does not enable sufficient palpation, it may appear more pronounced than in an ordinary stomach.

MUCOSAL ATROPHY

The roentgen signs of mucosal atrophy are a "dry stomach," and thin mucosal folds not exceeding 3–3.5 mm., with only slight tortuosity at the greater curvature (Fig. 1, *A* and *B*; Fig. 2*A*; Table I–III). If this is found in a case of histamine achylia, it suggests atrophy. Mostly there is a hook-

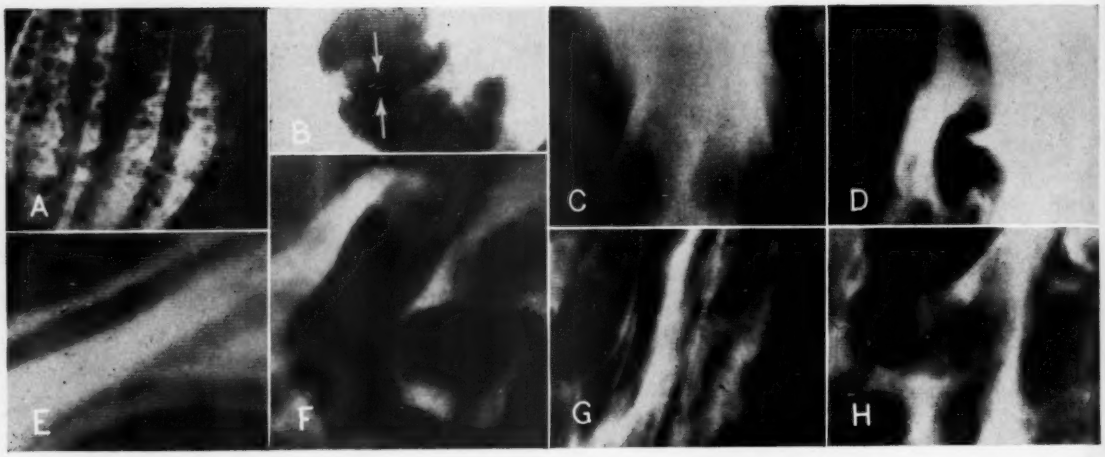

Fig. 2. Mucosal folds (description in text). (*A*) Thin folds of 2–2.5 mm., no tortuosity at greater curvature, granulation of barium. Folds measured in lower part of reproduction; in upper, they are flattened by too hard compression and would give confusing results. (*B, C*) Submucosal swelling and mucosal atrophy in gastric carcinoma of sinus (see Fig. 1*C* and 5*A*); (*C*) swollen thick folds in lower corpus, but (*B*) thin fold at angulus. (*D*) Folds of 4–4.5 mm. in extreme reddening of mucosa of gastroenterostomized stomach. (*E–G*). Swelling in stomach with gastroenterostomy (*E*) eight years ago before first operation, (*F*) same case, swelling at time of gastroscopy (see Fig. 5*C*), and (*G*) same case, ordinary folds after partial resection. (*H*) Swollen folds after partial resection (see Fig. 1*H*).

Table II

Mucosal folds on roentgen examination. Analysis of 213 cases. Numbers in parenthesis are cases with no other gastroduodenal disease

Gastroscopic Findings	Diameter of the mucosal folds								
	Less than 2.5 mm.	2.5–3 mm.	3–3.5 mm.	3.5–4 mm.	4–4.5 mm.	4.5–5 mm.	5–5.5 mm.	5.5–6 mm.	6 mm. and more
Mucosal atrophy, pronounced*	3 (3)	9 (5)	2 (2)	3 (1)†					
Mucosal atrophy, slight	2 (2)	3 (3)	4 (3)	2(1)	3 (2)				
Normal mucosa		4 (2)	23 (13)	27 (13)	18 (4)	3 (—)	1 (—)		
Catarrhal gastritis, reddening		6 (3)	14 (12)	15 (6)	14 (5)	1 (—)	2 (2)		
Catarrhal gastritis, swelling			1 (—)	4 (1)	6 (3)	3 (1)		4 (1)	3 (1)
Cobblestone mucosa			5 (1)	5 (—)	10 (4)	9 (1)	1 (—)	1 (—)	

* In 2 cases, the folds of an ectatic stomach were flattened and invisible.
† This was a case of atrophic-hypertrophic gastritis (Fig. 3).

formed stomach, but in some cases a vertical one is found.

It may appear that it is mainly the histamine achylia which has enabled the diagnosis. Achylia, however, may occur *without* atrophy.[5,25] Sometimes the roentgen signs point out a case *not* looking like atrophy. It is of clinical importance to determine this from a simple roentgen examination. In our material, this has occurred in 2 cases of histamine achylia. In the one there was a slight catarrhal and in the other an atrophic-hypertrophic gastritis (Fig. 3). Cases reported as achylia by the Ewald test meal, but not looking like atrophy roentgenologically, were frequently pointed out. This is easy where the folds exceed 3.5 mm. If they are less than 3.5 mm., it can be done only where the remaining roentgen signs are sufficiently characteristic; in our material, 1 case was not pointed out.

The roentgen signs have been developed as follows. In uncomplicated atrophy, the folds have not exceeded 3–3.5 mm. (Table II). Of the 3 cases with thicker folds, 2 had gastric tumors and, histopathologically, submucosal edema explaining the increased diameter, whereas 1 had a mixed type of gastritis interpreted as atrophic-hypertrophic. If the latter is excluded, 10 uncomplicated cases remain, of which 7 are covered by the roentgen signs (70 per cent). The percentage would be higher if a patient not repeatedly neglected the instruction to fast, and there was no "dry stomach." All this concerns cases with no other gastric disease than mucosal atrophy.

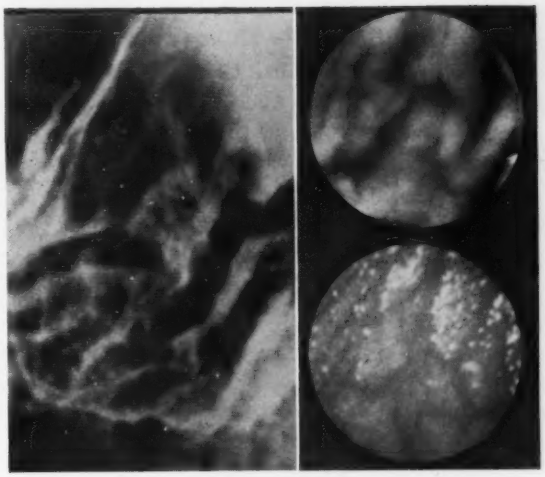

Fig. 3. Atrophic-hypertrophic gastritis. Folds of 3.5–4 mm., irregular areolae. Roentgenogram and aimed gastroscopic photographs.

Table III

Intermediary fluid and secretion on roentgen examination. Analysis of 213 cases. Numbers in parenthesis are cases with no other gastroduodenal disease

Gastroscopic Findings	Number of Cases	Intermediary Fluid			Secretion		
		Dry stomach	Slight	Medium or high	None	Ordinary	Hyper-secretion
Mucosal atrophy, pronounced	19	9 (8)	6 (3)	4 (—)	12 (9)	6 (1)	1 (1)
Mucosal atrophy, slight	14	7 (7)	4 (3)	3 (1)	7 (7)	6 (3)	1 (1)
Normal mucosa	76	6 (5)	37 (16)	33 (12)	16 (7)	47 (20)	13 (6)
Catarrhal gastritis, reddening	52	14 (9)	27 (18)	11 (1)	18 (12)	26 (15)	8 (1)
Catarrhal gastritis, swelling	21		9 (4)	12 (3)	3 (1)	15 (5)	3 (1)
Cobblestone mucosa	31	1 (—)	12 (4)	18 (2)	4 (1)	18 (5)	9 (—)

The results are different if there is a gastric tumor also. Because of submucosal swelling, frequent in tumor cases, the folds may be thickened, and there is frequently some fluid in the fasting stomach which no longer appears "dry." In stenosing prepyloric tumor the stomach may be distended to a degree where the folds are flattened and invisible; in such a case, a good mixture of the barium with the fluid on palpation can be used as a sign of atrophy (Fig. 1, *D* and *E*). In atrophic mucosa, the folds usually are flattened when the stomach is distended by retention, a parallel to the gastroscopic sign of flattened folds in atrophy on inflation of the stomach with air.

Of the 8 cases of atrophy, complicated by gastric tumor, only 3 showed the roentgen signs (37 per cent). Increased experience will probably enable one to guess where only some of the signs are present. For instance, thin folds in some parts of the stomach, with thick swollen folds dominating the picture, may permit a deduction (Fig. 2, *B* and *C*).

Exceptionally, highly tortuous folds at the greater curvature are found in atrophy. Pronounced granulation of the barium (Fig. 2*A*) is only found in atrophy, whereas moderate granulation has occurred in any group.

A number of cases other than atrophy have folds less than 3.5 mm. These have to be excluded by the remaining roentgen signs and by the presence of free gastric acidity.

SLIGHT MUCOSAL ATROPHY

Gastroscopically, slight mucosal atrophy contains a number of borderline cases, and even the roentgen findings are polymorphous. On gastroscopy, there were translucent submucosal vessels but the finer branches, especially the fine reddish network, were not to be observed. Some of these probably have a normal mucosa, as translucent vessels may be observed in histologically normal parenchyma.[27a] Free acidity was found in 2 of the 10 uncomplicated cases, which thus were excluded. Of the remaining, 5 are covered by the roentgen signs of atrophy (63 per cent).

In slight atrophy, combined with gastric tumor, only 1 of the 4 cases was covered by the roentgen signs.

NORMAL MUCOSA

In the current work of a roentgen department, most cases are interpreted as normal. One should not attempt to classify every case in some pathological group, but to look for cases sufficiently characteristic to be differentiated from the bulk of the material.

In most normal cases, there has been a slight intermediary fluid. A "dry stomach," as in the uncomplicated cases of atrophy, was found in 6 of the 76 normal cases, of which 2 even had folds less than 3.5 mm. and had to be separated from atrophy by the histamine test.

Hypersecretion (Fig. 1*F*) is not a sign of gastritis; neither are highly tortuous folds (irritation relief) a sign of gastritis.

CATARRHAL GASTRITIS

Of the 73 cases of catarrhal gastritis, 52 have a reddened mucosa, whereas in 21 the mucosa has been swollen or, in some instances, apparently hypertrophic, with or without moderate reddening.

A. *Catarrhal Gastritis with Reddening* is not diagnosed roentgenologically, as the signs are indefinite.

The roentgen signs of reddening are a hook-formed stomach, without or with only slight intermediary fluid, ordinary or good adherence of the barium to the mucosal surface, no increased secretion, and mucosal folds of about the normal size. In cases with even a gastric ulcer or tumor, influencing the roentgen signs, the findings are variable.

The hook-formed, shorter stomach is probably due to increased tonus. This would agree with the observation[13,20] that, while performing a gastroscopy, the stomach in catarrhal gastritis is frequently more difficult to inflate than in the normal. A

"dry stomach" is frequent where there is a reddened mucosa and a grayish nontranslucent superficial mucous layer on gastroscopy; the roentgen finding may resemble atrophy, and a histamine test may be needed for differentiation. Reddening is not to be sought among cases with thick folds. Although statistical analysis reveals a slight thickening, it is not sufficient for diagnosis. For instance, in a case of extreme reddening (Fig. 2*D*), there were folds of 4–4.5 mm. which had measured 3–3.5 mm. on a former examination. On the contrary, in a case of extremely thickened folds there is usually a moderate reddening only or none (Fig. 2*F*). These two extreme cases have been selected among gastroenterostomies, where the gravest gastritis is to be found. The same, less pronounced, is found in the stomach not operated on.

The increased tonus of the stomach is an indirect sign, even found in swelling, and sometimes in the remaining gastroscopic groups. Although varying in length from case to case, the hook-formed stomach is, in general, slightly shorter than in the remaining groups.

B. *Catarrhal Gastritis with Swelling.* Contrary to reddening, catarrhal gastritis with swelling is frequently identified roentgenologically, a fact of clinical importance.

The roentgen signs of swelling are mucosal folds of at least 5 mm. in diameter, usually in a hook-formed stomach with intermediary fluid (Table I–III). The signs cover 33 per cent of the cases. There is frequently an intermediary fluid, contrary to reddening where fluid is lacking or only slight. Apparently swelling causes a functional disturbance of the gastric emptying.

The roentgen diagnosis of swelling is based on thickened folds (Fig. 2, *C*, *F* and *H*). The size of the folds depends on two factors: the glandular parenchyma of the mucosa, and the submucosa (Table IV). Where there is a voluminous parenchyma histologically, the roentgen examination reveals a greater diameter of the folds than in medium-sized parenchyma. On the other hand, submucosal swelling may cause a severe thickening of the folds. Various combinations of these two factors may occur. The cases with folds of 4–4.5 mm. of Table IV, for instance, include some with a voluminous parenchyma but without any submucosal swelling, and others with a small parenchyma but a grave submucosal swelling. A case of mucosal atrophy, with submucosal swelling, may have folds as thick as 5.5–6 mm., although in uncomplicated atrophy they would not exceed 3–3.5 mm. The thickest folds in a voluminous parenchyma, without swelling, seem to be 5 mm.*

In the literature, confusion has been caused by not separating submucosal swelling and changes of the glandular parenchyma. A search of the photomicrographs and records of cases published as hypertrophic gastritis[2,3,12,23] reveals in most cases a pronounced swelling. The term hypertrophic gastritis, as used in the literature, is indefinite. In the present analysis, cases formerly classified as hypertrophic gastritis are classified gastroscopically as catarrhal gastritis or as cobblestone mucosa.

If we return to the gastroscopic findings, the thickest folds in normal mucosa are 5.5 mm. (Table II). This, however, seems to include cases of unrecognized submucosal swelling, probably present even in the other gastroscopic groups. Submucosal swelling is not directly diagnosed gastroscopically and may only be guessed by the size and the appearance of the folds. There is no regular connection of submucosal and superficial swelling (Table IV). The gastroscopic appearance of the mucosa does therefore not permit any direct conclusion as to the submucosa. Superficial swelling seems to cause only an insignificant thickening of the folds.

The roentgen signs may even complete the gastroscopic method. Gastroscopically, Figure 4 is mucosal atrophy. Roentgenologically, however, there were thickened

* Table IV reveals a regularity indicating that histologic artefacts by the trauma of the operation, as in animals under experimental conditions,[26] are not significant in a resection specimen of the clinic.

TABLE IV

MUCOSAL FOLDS ON ROENTGEN EXAMINATION, COMPARED TO HISTOLOGIC FINDINGS. ANALYSIS OF 42 UNSELECTED CASES. DESCRIPTION IN TEXT

Case Number	Mucosal Folds	Glandular Parenchyma of Mucosa	Swelling		Gastroscopy
			Sub-mucosal	Super-ficial	
1	2.5–3 mm.	Atrophic	+	o	Atrophy
2	3–3.5 mm.	Atrophic	+	+	Atrophy
3	3–3.5 mm.	Atrophic	++	+	Atrophy
4	3–3.5 mm.	Atrophic	++	o	Slight atrophy
5	3–3.5 mm.*	Atrophic	+++	o	Atrophy
6	3–3.5 mm.	Small	++	o	Slight atrophy
7	3–3.5 mm.	Medium	o	+	Normal
8	3–3.5 mm.	Medium	o	o	Normal
9	3–3.5 mm.	Medium	++	o	Cobblestone-mucosa
10	3–3.5 mm.	Large	o	o	Normal
11	3.5–4 mm.	Atrophic	++	o	Slight atrophy
12	3.5–4 mm.	Moderate atrophy	++	o	Normal
13	3.5–4 mm.	Small	++	++	Reddening
14	3.5–4 mm.	Small	o	o	Reddening
15	3.5–4 mm.	Medium	+	o	Reddening
16	3.5–4 mm.	Medium	+	o	Normal
17	3.5–4 mm.	Medium	++	o	Cobblestone-mucosa
18	3.5–4 mm.	Medium	++	+	Slight atrophy
19	3.5–4 mm.	Large	+	o	Cobblestone-mucosa
20	3.5–4 mm.	Large	+	++	Normal
21	4–4.5 mm.	Small	++	o	Normal
22	4–4.5 mm.	Small	++	+	Swelling
23	4–4.5 mm.	Small	+++	+	Swelling
24	4–4.5 mm.	Medium	o	(+)	Normal
25	4–4.5 mm.	Medium	o	+	Cobblestone-mucosa
26	4–4.5 mm.	Medium	+	(+)	Swelling
27	4–4.5 mm.	Medium	+	++	Slight atrophy
28	4–4.5 mm.†	Medium	+	+	Reddening
29	4–4.5 mm.	Medium	++	(+)	Cobblestone-mucosa
30	4–4.5 mm.	Medium	++	+	Normal
31	4–4.5 mm.	Large	o	o	Normal
32	4–4.5 mm.	Large	+(+)	o	Cobblestone-mucosa
33	4–4.5 mm.	Large	o	+	Cobblestone-mucosa
34	4–4.5 mm.	Large	(+)	o	Cobblestone-mucosa
35	4.5–5 mm.	Atrophic	++++	(+)	Atrophy
36	4.5–5 mm.	Large	o	o	Cobblestone-mucosa
37	4.5–5 mm.	Large	+	o	Reddening
38	4.5–5 mm.	Large	+	(+)	Cobblestone-mucosa, erosions
39	5–5.5 mm.	Medium	+++	o	Normal
40	6 mm. and more	Medium	++++	(+)	Pale swelling
41	6 mm. and more	Large	++	+	Swelling, erosions
42	6 mm. and more	Large	+++	++	Swelling, erosions

* Gastric stump after partial resection.
† Biopsy.

folds, interpreted as swelling; the patient was operated on a year later for antral carcinoma, and the resection specimen revealed a grave submucosal swelling histologically, and a carcinomatous lymphangitis even distant to the tumor. Apparently the influence of submucosal swelling on the gastroscopic findings has not been described in the literature. In our material, swelling has not influenced the gastroscopic visibility of the submucosal blood vessels in atrophy or the color of the mucosa of the inflated stomach. Theoretically, swelling can be guessed on inspection of the folds in the beginning of the gastroscopy, before the stomach is inflated and the folds are flattened. The confusing statement in the literature that the roentgen findings in atrophy are unreliable is caused by not separating submucosal swelling and glandular parenchyma.

On follow-up of a case, slight variations in size of the mucosal folds may suggest swelling even where the folds do not reach 5 mm. These variations, probably mostly caused by swelling, are to be interpreted

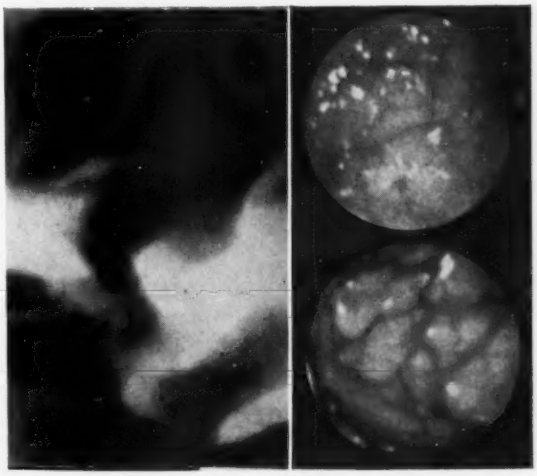

Fig. 4. Extreme swelling of antral submucosa in atrophy. Description in text.

with caution, as nothing is known as to the rapidity and extent of glandular hyperplasia of the human stomach. In animal experiments, hyperplasia has been obtained in two to four weeks[7,9] and in nine weeks.[17]

Irregular, thick folds, varying in diameter in different parts of the stomach, indicate swelling. In extreme swelling, there may be extremely thickened and tortuous folds resembling gyri.

In swelling, there has frequently even

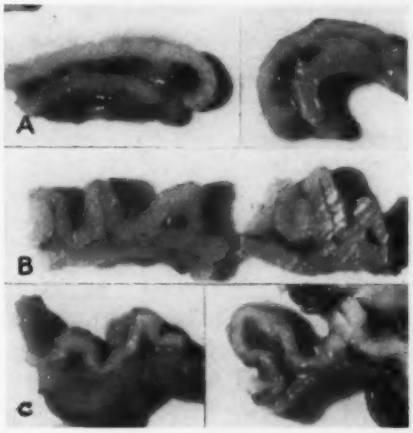

Fig. 5. Submucosal swelling and size of folds (sections of gastric wall, fixed in formalin). (*A*) Grave submucosal swelling in atrophy (see Fig. 1*C* and Fig. 2*B* and *C*). (*B*) No submucosal swelling, voluminous glandular parenchyma. (*C*) Grave submucosal swelling, average size of parenchyma (see Fig. 2*F*).

been some other gastroduodenal disease, contrary to reddening which mostly has been uncomplicated. Apparently swelling is mostly connected with ulcer or tumor, extending not only to the close proximity of the lesion but involving wide areas of the stomach. Swelling is thus an indication to search for ulcer or malignancy and, if necessary, to keep a case under observation. In the literature, some cases of grave swelling have not had any malignancy on histopathologic examination of the resection specimen,[2] indicating that grave swelling even may occur independently of ulcer or tumor. In 4 of our cases, there have been multiple erosions; these will be published in another paper.

Except for the glandular parenchyma and the submucosal swelling, a third factor may influence the size of the folds. The submucosa and the mucosa may be infiltrated by sarcoma,[10,16,22,27e] leukemia[24] and lymphogranulomatosis.[6,19] There may be a

TABLE V

THE ROENTGEN SIGNS OF GASTRITIS ON REPEATED EXAMINATION. ANALYSIS OF 119 UNSELECTED CASES

Gastroscopic Findings	Number of Cases	Number of Examinations	Roentgen Findings on Repeated Examination			
			Identical	Changes of the		
				Gastric configuration	Intermediary fluid and secretion	Mucosal folds
Mucosal atrophy, pronounced	9 (5)	24 (16)	5 (2)	2 (2)	2 (1)	1 (1)
Mucosal atrophy, slight	3 (3)	6 (6)	2 (2)		1 (1)	1 (1)
Normal mucosa	48 (17)	159 (55)	17 (4)	8 (4)	20 (6)	23 (10)
Catarrhal gastritis, reddening	33 (15)	108 (37)	11 (8)	12 (6)	14 (5)	19 (5)
Catarrhal gastritis, swelling	8 (1)	27 (2)	1 (—)	3 (—)	4 (—)	6 (1)
Cobblestone-mucosa	18 (3)	59 (15)	3 (—)	3 (—)	14 (3)	13 (2)

severe thickening and stiffness of the folds, different from ordinary gastritis on roentgen examination. Gastroscopy may permit the diagnosis,[27e] and the basic disease may give clue to interpretation.

COBBLESTONE MUCOSA

In cobblestone mucosa, the roentgen signs are not sufficiently characteristic. Contrary to what might be expected, the gastric areolae do not permit a roentgen diagnosis, which is explained by the conditions causing the gastroscopic picture of cobblestone mucosa.[27d] Roentgenologically, the gastric areolae may be visualized in various gastroscopic groups, even in some cases of atrophy (Fig. 3) and, on the other hand, a cobblestone mucosa may have a flat surface on the roentgenogram.

A vertical stomach is more frequent in cobblestone mucosa than in any other group. In most cases, there have been folds of 4 mm. or more, and intermediary fluid and hypersecretion have been frequent.

CONSTANCY AND VARIATIONS OF THE ROENTGEN SIGNS

On repeated roentgen examination (Table v), variations of the gastric configuration have been most frequent in catarrhal gastritis with reddening. The next frequent has been swelling, contrary to cobblestone mucosa where the gastric configuration has been relatively constant. This would agree with the interpretation of the hook-formed stomach, in reddening and swelling, as increased tonus.

The mucosal folds have been most variable in swelling and in cobblestone mucosa, but even in reddening the variations have been more frequent than in normal.

In general, the roentgen findings have been most constant in mucosal atrophy.

FACTORS INFLUENCING THE ROENTGEN SIGNS

Except for the size of the mucosal folds, the roentgen signs of gastritis are indirect

signs, influenced by other factors than gastritis only.*

In underweight, a vertical stomach is slightly more frequent than in normal and in overweight. If account is taken of this fact, the interpretation of the gastric configuration can probably be improved. In our material, however, this difference is slight and does not essentially alter the regular findings in gastritis.

Drugs may influence the stomach.[1,8,28] In our material, antacids and antispasmodics, combined with dietetic treatment, have been the most important; hypersecretion frequently disappeared and the intermediary fluid was reduced after treatment. Our patients have received atropine or extract of belladonna, and sometimes papaverine and small doses of luminal. In current work, other drugs seem to be less important. Morphine, insulin and ipecac, for instance, have not been used in our material.

The vegetative nervous system, the cause of hypotonia after vagotomy[15,18] and apparently of idiopathic dilatation of the stomach,[4] seems even to be the cause of the increased tonus in catarrhal gastritis and of the long hypotonic stomach in some of our normal cases. Irritated, tortuous folds seem to depend on the vegetative regulation. External, *e.g.*, auditory stimuli[14b] or fear[14c] have been found to influence the stomach.

If the mucosal folds are measured before onset of the peristalsis, the autoplastic movements of the mucosa seem to cause no significant variation in diameter of the folds.

CLINICAL SYMPTOMS

In our material, the clinical symptoms of the different types of gastritis are not sufficiently characteristic to be used together with the roentgen signs.

* To avoid uncontrollable irritation, laxatives and enema, proposed by some authors before a roentgen examination of the stomach, have not been used.

GASTROENTEROSTOMY

The gravest gastritis, in our material, is in the stomach with a gastroenterostomy. The roentgen signs are the same as in the stomach,[4] seems even to be the cause of the increased tonus in catarrhal gastritis and of the long hypotonic stomach in some of our normal cases. Irritated, tortuous folds seem to depend on the vegetative regulation. External, *e.g.*, auditory stimuli[14b] or fear [14c] have been found to influence the stomach.

PARTIAL RESECTION

Depending on the surgical technique, the shape of a resection stump is variable. Of the roentgen signs, the mucosal folds are measured and recorded as in a stomach not operated on. The intermediary fluid is usually lacking. Submucosal swelling, however, may cause a moderate intermediary fluid even in a resection stump, without any stenosis to be found (Fig. 1*H*). In general, the folds of a gastric stump have the same diameter as before the operation, but considerable differences are to be found where a gastritis has developed in the resection stump, or where a preoperative gastritis has disappeared after resection. In 15 of our 23 cases, the folds of the resection stump were of the same size as before the operation, falling in the range of 2.5 to 4.5 mm. In the remaining 8, the folds of the stump and those before the operation (numbers in parenthesis) were the following: 5.5–6 mm. (Fig. 2*H*) (4–4.5 mm.); 5–5.5 mm. (4–4.5 mm.); 4.5–5 mm. (3.5–4 mm.); 4.5–5 mm. (3–3.5 mm.); 4–4.5 mm. (4.5–5 mm.); 3.5–4 mm. (4–4.5 mm.); 3–3.5 mm. (3.5–4 mm.); and 3–3.5 mm. (Fig. 2*G*) (8–10 mm., there was a gastroenterostomy, Fig. 2*F*).

SUMMARY

In mucosal atrophy, 70 per cent of the uncomplicated cases are covered by the roentgen signs "dry stomach" and mucosal folds not exceeding 3–3.5 mm., in a case of histamine achylia. If, however, atrophy is

combined with a gastric tumor, a submucosal swelling frequently alters the roentgen picture, and a characteristic appearance is found in 37 per cent only.

On the other hand, there are cases of histamine achylia *not* resembling atrophy roentgenologically. This permits pointing out achylia caused by other factors than atrophy, mixed forms of atrophy, and the clinically important combination of atrophy and swelling which is an indication to search for malignancy.

In slight mucosal atrophy, a borderline group which even contains normal cases, 63 per cent of the uncomplicated cases are covered by the roentgen signs.

Catarrhal gastritis with reddening and cobblestone mucosa are not to be diagnosed roentgenologically.

Catarrhal gastritis with swelling is identified by thickened folds of 5 mm. or more, which cover 33 per cent of all cases. Furthermore, moderate swelling may be identified where there is a change in size of the folds on follow-up examination. In submucosal swelling, there is usually a moderate intermediary fluid, apparently by functional disturbance (contrary to reddening, where intermediary fluid is lacking or there is a small amount only in uncomplicated cases); this is even noted in swelling in the stump of a partially resected stomach.

The method of measurement of the mucosal folds is important and is described in detail.

The roentgen findings complete the gastroscopic method in the diagnosis of submucosal swelling, which is not to be directly diagnosed by gastroscopy.

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PSEUDOTUMORS OF THE DUODENAL BULB*

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THE distinction between primary tumors of the duodenal bulb and pseudotumors of this area is frequently difficult. The not infrequently encountered filling defect in the bulb is generally regarded as one of many benign tumors, such as myoma, polyp, fibroma, lipoma, angioma, cyst, varices or aberrant pancreatic nodule.

Probably the most frequent pseudotumors of the bulb are hypertrophic polypoid duodenitis, herniation of redundant gastric mucosa into the base of the bulb, and pedunculated gastric polyp arising from the antrum prolapsing through the pylorus, all of which present as filling defects, when the duodenal bulb is examined roentgenographically.

We would like to present an additional group of pseudotumors of the bulb which are interesting in their roentgen similarity to the true tumors of this area, but which pathologically were proved to be more apparent than real. Simultaneously, a discussion of differential roentgen characteristics might be of value in affording aid to the diagnosis of these pseudotumors.

REPORT OF CASES

CASE 1. *Pedunculated Tumor Arising from the Gastric Cardia, Prolapsing into the Duodenal Bulb.*

The patient was a female, aged fifty-six, with a long history of epigastric pain, nausea and vomiting of a periodic nature. Recurrent melena, moderate secondary anemia, and normal gastric acidity were found. Physical examination was essentially negative.

Roentgen examination revealed a large intraluminal filling defect in the duodenal bulb and extensive deformity of most of the lesser curvature of the stomach (Fig. 1). The bulb defect was surrounded by intact walls in both sagittal and lateral views (Fig. 2 and 3). This, plus a lack of displacement of the bulb, indicated the defect to be due to an intraluminal process.

The extensive deformity of the lesser curvature aspect of the stomach was not correctly evaluated, preoperatively. The intact mucosa excluded an infiltrating lesion of the stomach. Though we favored extrinsic pressure, possibly by extensive metastatic lymph node involvement, again the lack of displacement and the

FIG. 1. Case 1.

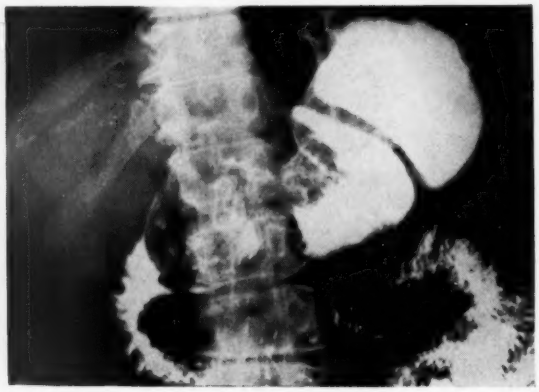

FIG. 2. Case 1.

* From the Department of Roentgenology, Albert Einstein Medical Center, Northern Division, Philadelphia, Pennsylvania.

normal flexibility and mobility of the gastric walls were factors against such a contention. At surgery, a distended but intact duodenal bulb, with prolapse of much of the gastric lesser curvature, was found. Following manipulation of the tumor mass back through the pylorus, the gastric lesser curvature was seen to be intact. A very limited wedge resection of the cardiac end of the stomach, at the site of attachment of the pedicle, was adequate in removal of the pedunculated leiomyoma.

Comment. It became evident that had we been able to reduce the duodenal tumor back into the stomach, or had we appreciated a pedicle, a preoperative diagnosis should have been evident. This case emphasizes the fact that pedunculated gastric tumors may arise from any part of the stomach, and though they generally arise from the antrum, they occasionally have their base in the cardia or body and cause considerable traction deformity of the gastric wall. The traction on the gastric wall may be so extensive as to cause it to also be prolapsed through the pylorus and present as a pseudotumor in the duodenum. Certainly, an intrinsic tumor of the proximal duodenum associated with deformity of the gastric lesser curvature, no matter how extensive, might well be caused by a pedunculated and prolapsing gastric tumor. This pseudotumor of the duodenal bulb is somewhat similar in its appearance to prolapsing gastric mucosa. However, the characteristic defect noted in the base of the cap, in the latter, and the identification of a pedicle in the former should permit differentiation of these two pseudotumors of the duodenal bulb.

Case II. *Duodenal Diverticulum Adherent to the Wall of the Duodenal Bulb.*

The patient was a male, aged fifty-seven, admitted with subsiding jaundice and a long history of postprandial distress. Physical examination revealed right upper quadrant tenderness. Doubly intensified oral cholecystography demonstrated a nonfunctioning gallbladder. An upper gastrointestinal examination revealed a constant small smooth defect in the duodenal bulb midway between base and apex on its greater curvature aspect (Fig. 4 and 5). At no time, was a diverticulum filled with barium identified. A diverticular neck was only vaguely suggested. Though the latter finding suggested that an unusual diverticulum was the most likely diagnostic possibility, re-examination was deemed advisable to exclude the possibility of an intramural tumor such as myoma or an aberrant pancreatic rest. However, before that could be performed, surgery for emergency cholecystectomy was done. This also revealed a duodenal diverticulum, whose neck arose from the peri-ampullary area and its fundus to be actually adherent to the duodenal bulb by several fibrous strands. This confirmed our impression that an adherent diverticulum to the wall of the bulb caused the pseudotumor, noted in the preoperative study.

Fig. 3. Case I.

Comment. It is not unusual for a duodenal diverticulum not to fill with barium. This is generally attributed to the presence of food, nonopaque residue, or as has been noted on rare occasions, tumor within a diverticulum. The latter cause is generally differentiated from the former by its constancy and expansile character. It is evident that this specific case, with its duodenal diverticulum that did not fill with barium, and which presented as a possible pseudotumor of the bulb, is explained as follows:

Fig. 4. Case II. Duodenal diverticulum overlying and adherent to the duodenal bulb.

The bulb, when distended with barium, acted as a ball valve effect on the adherent diverticulum, compressing it, and thereby preventing barium from entering the fundus of the diverticulum. The adherent, non-filled diverticulum, in turn, appears as a filling defect in the wall of the bulb.

Case III. *A Small Acute Duodenal Ulcer Surrounded by an Intense Perifocal Edematous Reaction.*

A forty-one year old wife of a physician with intermittent episodes of right upper quadrant pain, nausea and vomiting, best relieved by self-induced vomiting, was seen as an outpatient. Physical examination was essentially negative. The stool examination was positive for occult blood. Roentgen examination revealed a constant, sharply circumscribed filling defect, 1.5 cm. in diameter situated in the midline of the duodenal cap (Fig. 6). The bulb had a normal size, and the remainder of the mucosal pattern was intact. It was slightly tender and irritable. Mobility was normal. The filling defect was constant in location and could not be displaced by palpation. Slight increase in the width of the pylorus was noted, and slight delay in gastric emptying was also noted. A pedicle was not identified, and a tentative diagnosis of a sessile mucosal polyp arising from the bulb was entertained. The normal appearance of the distal antral mucosal pattern and the lack of deformity of the base of the bulb were findings against its representing herniation of gastric mucosa through the pylorus. Its singular appearance spoke against it representing hypertrophy of Brunner's glands, and the lack of displacement of the walls of the bulb argued against extrinsic pressure by a lymph node.

Though re-examination was scheduled, the patient was admitted to the hospital and surgery performed before that could be done. A small, sharply circumscribed area of stippling and induration of the duodenal wall surrounding a very tiny and almost completely healed ulcer was found. A duodenostomy was performed, but no evidence of an intraluminal tumor was present. It is evident that had comparative evaluation of the above patient, following an interval of ten to fourteen days of intensive medical therapy, been carried out, the diagnosis would have become obvious and this patient spared needless surgery.

Comment. This pseudotumor of the bulb was caused by the sharply circumscribed perifocal edematous reaction attendant on a small duodenal ulcer. It illustrates how the actual fleck may not be visible due to the overhanging edematous mucous membrane about the ulcer, and the roentgen diagnosis of an ulcer crater, therefore, not apparent.

Case iv. *Gallstone Impacted into Wall of the Bulb with Pseudotumor Appearance.*

The patient was a female, aged sixty-one, with a long history of epigastric pain and vomiting for at least the past six years, which had become worse in the past six months, associated with weight loss of 25 lb. The stools were positive for occult blood. Physical examination revealed a poorly defined epigastric mass A moderately severe secondary anemia was present.

Fig. 5. Case ii. Duodenal diverticulum presenting as "pseudotumor" in the bulb.

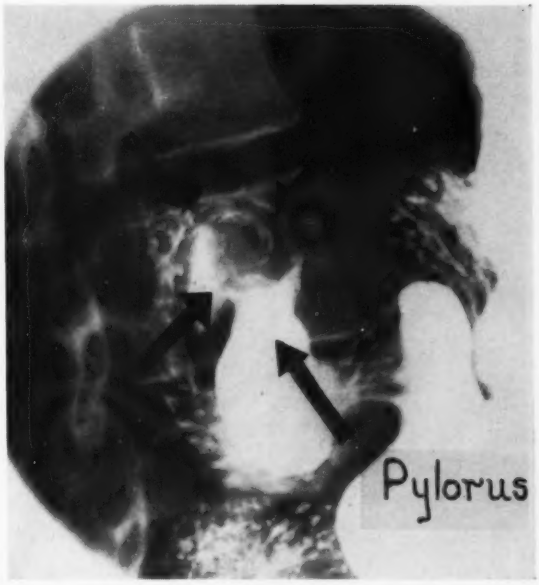

Fig. 6. Case iii. A small acute ulcer in the bulb with an intense perifocal edematous reaction presenting as a pseudotumor. The right lower arrow identifies a slightly dilated pylorus. The other three arrows outline the filling defect in the bulb.

Roentgen examination revealed a large sharply circumscribed filling defect in the distal aspect of the duodenal bulb. (Fig. 7 and 8). The remainder of the mucosal pattern of the bulb appeared intact. The bulb was not dis-

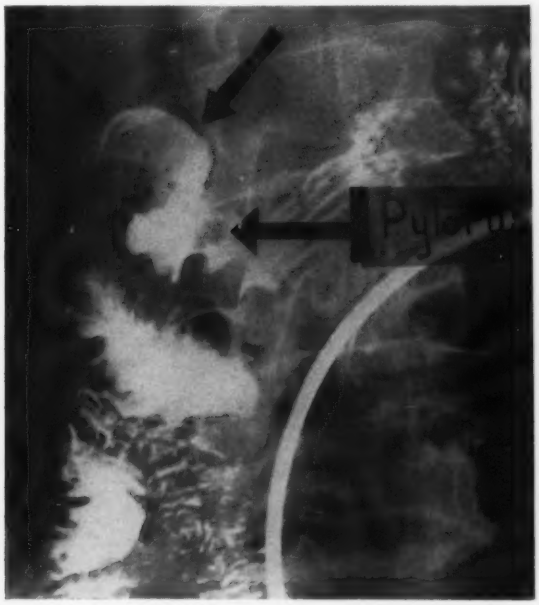

Fig. 7. Case iv. Gallstone impacted into the duodenal bulb.

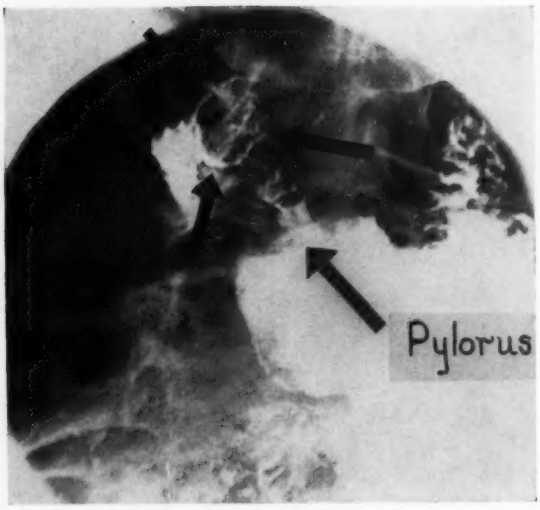

Fig. 8. Case iv. Gallstone impacted into the wall of the duodenal bulb.

placed, irritable or tender, and it appeared slightly limited in its mobility. The defect was constantly situated near the apex of the bulb and could not be moved or displaced by manual palpation. These findings, as well as the lack of a demonstrable pedicle, were findings against a prolapsing tumor. Doubly intensified oral cholecystography demonstrated a nonfunctioning gallbladder.

Our differential diagnostic possibilities were between an intramural process such as myoma or a pancreatic rest and extrinsic involvement by a gallstone or lymph node. Theoretically, one notes an intact wall about the intramural lesions, whereas the extrinsic process should produce a slight displacement of one wall and have associated limitation of mobility. Actually, the distinction of origin between extrinsic and intramural tumors can be quite difficult.

At surgery, the gallbladder was markedly adherent and could not be completely removed. A dense hard mass within the bulb was exposed by the surgeon. It was his first impression that he was dealing with a primary nonresectable malignancy of the bulb. Only after extensive dissection was he able to expose and remove a large gallstone that was burrowed into the intramural aspect of the bulb, accounting for the pseudotumor of the bulb noted in the preoperative roentgen examination.

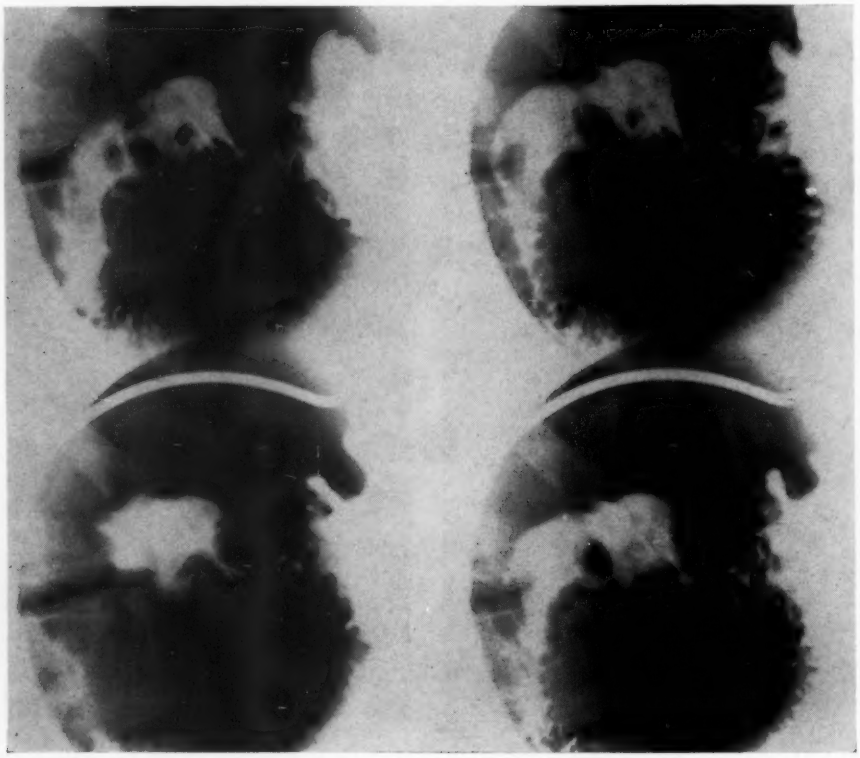

Fig. 9. Case v. Hypertrophy of Brunner's glands.

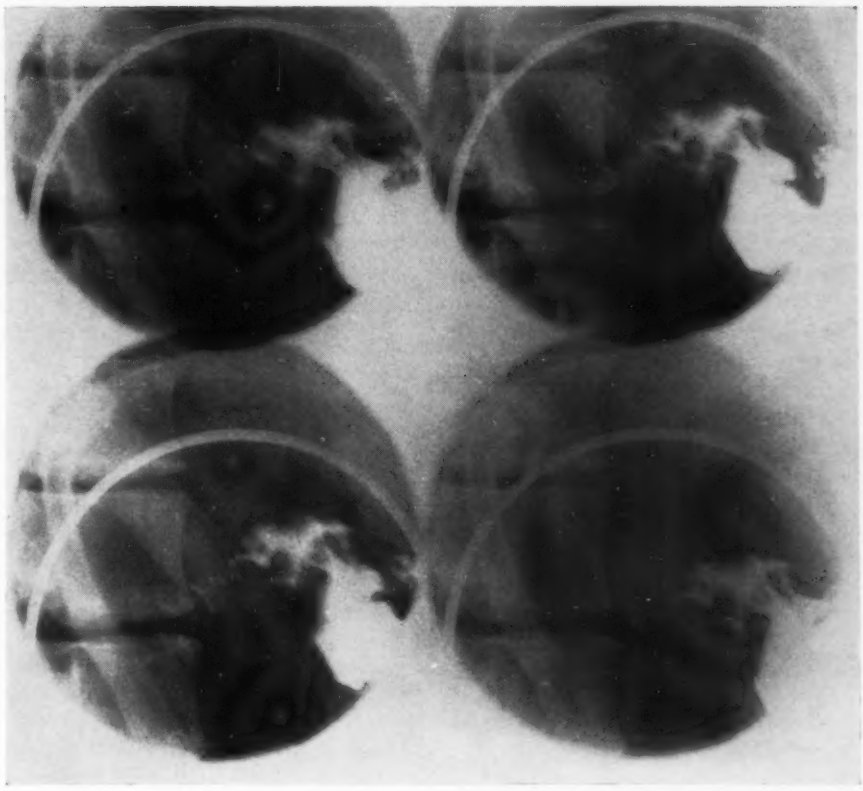

Fig. 10. Case v. Hypertrophy of Brunner's glands.

Case v. *Hyperplasia of Brunner's Glands.*

A forty year old male was admitted to the hospital for investigation of right lower quadrant distress of one year's duration and a longer history of epigastric postprandial distress occurring about one-half to one hour following meals, occasionally relieved by antacids and seemingly related to highly seasoned foods. A lack of normal mobility and separability of the terminal ileum from the cecum and a history of a previous appendectomy suggested localized nonobstructing adhesions as the cause of the right lower quadrant distress.

In the examination of the stomach and duodenum, multiple large and moderate-sized filling defects suggesting multiple polypoid tumors were noted occupying the entire bulb (Fig. 9). These were constantly situated in the bulb which was normally movable and not irritable. The actual size would vary somewhat in different serialographic exposures, depending upon the degree of compression indicating the masses to be compressible and probably intramural in orgin. The remainder of the entire gastrointestinal tract was otherwise negative. This patient was not operated upon, and the actual diagnosis in this case is a matter of conjecture. A fractional gastric analysis showed a fasting acid of 105 units of free acid and 117 units of total acid.

The appearance of these filling defects, the high gastric acid, and slightly changeable size on compression serialographic exposures, normal mobility of the bulb, and the apparent slight decrease in the size of the defects when re-evaluated following three months of intensive medical therapy (Fig. 10) strongly suggest that this case represents hyperplasia of Brunner's glands. Another feature indicating that this case represents hyperplasia of Brunner's glands is that the filling defects are largest adjacent to the pylorus and smaller in the distal bulb and proximal portion of the descending limb of the duodenum. Gray's anatomy states that these glands are limited to the duodenum and are in the submucous areolar tissue. They are largest and most numerous near the pylorus, gradually diminishing in number and size in the distal duodenum. In a proved and operated case of hyperplasia of Brunner's

glands, reported by Erb and Johnson, this diminution in size and number in reference of the pylorus is also well illustrated.

Since the cause of this increase in the size of Brunner's glands is believed to be a response to gastric hyperacidity, it was interesting to note that comparative studies, following therapy, suggest that there may be some decrease in the size of these pseudotumors.

The differential diagnosis in this case is polyposis of the duodenum, multiple benign tumors such as lipomatosis or hemangiomas or hypertrophic polypoid duodenitis. We believe the clinical and roentgen findings aided by the high gastric acidity, negative occult blood in the stools, and slight, but definite, response to antacid therapy causing slight decrease in size would probably indicate that the cause of the pseudotumors in this instance is hyperplasia of Brunner's glands.

SUMMARY

A group of pseudotumors in the duodenal bulb are presented, in order to emphasize the suspected intrinsic mass lesion that is more apparent than real. Cases of pedunculated tumor arising from the gastric cardia, duodenal diverticulum adherent to the wall of the duodenal bulb, small acute duodenal ulcer with perifocal edema, gallstone impacted into the wall of the duodenal bulb and a probable case of hyperplasia of Brunner's glands have been presented and illustrated.

Though tumors of the bulb are quite similar, in many respects, to tumors involving other portions of the gastrointestinal tract, roentgen examination is more prone to suggest pseudotumors in the former area than in the rest of the gastrointestinal tract. After careful application of the usual diagnostic criteria of circumscribed mucosal involvement, displacement of one wall, fixation or lack of normal mobility, an intact wall surrounding the tumor and obstruction with proximal dilatation, we have been impressed by the occasional difficulty in differentiating between true and pseudotumors of the duodenal bulb.

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Vol. 74, No. 4

ROENTGEN MANIFESTATIONS OF NECROTIZING GRANULOMATOSIS AND ANGIITIS OF THE LUNGS

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THERE have appeared with increasing frequency in the literature reports of a complex of granulomatosis with angiitis of the lungs, massive necrosis of the spleen and focal granulomatous glomerulonephritis. In these cases, which have received many interpretations and diagnoses because of their varied manifestations, there has been only sparse mention of the roentgen manifestations. Recently Fienberg[1] has described 2 typical examples of this condition which he called necrotizing granulomatosis and angiitis. In the present article, the roentgen findings in these 2 cases as well as those in a third case where the disease was limited to the lungs,[2] are described, and the few roentgenological descriptions in the literature are reviewed. The roentgen features of this disease, although based on very few observations, are presented in order to make radiologists more aware of this condition, and to aid in its detection.

CASE REPORTS

CASE 1. A twenty-seven year old white man was admitted to the hospital on July 28, 1950 with complaints of hemoptysis of 1/4 cup four months ago, weight loss of 20 lb., night sweats and pain in the left chest for the past eight months. Six years ago he had been treated in the Army for pneumonia and following this he had treated himself with sulfonamide for about a year for cough and fever. There was no history of allergy. On admission, there were physical signs of consolidation in the left lung base. No evidence of kidney disease was present. The white blood cell count was 11,600 per cu. mm. with 1 per cent eosinophils.

Initial film of the chest revealed a cavity about 3 cm. in diameter (Fig. 1) containing fluid within a poorly demarcated area of consolidation in the posterior basal segment of the left lower lobe. The walls of the cavity were not clearly defined.

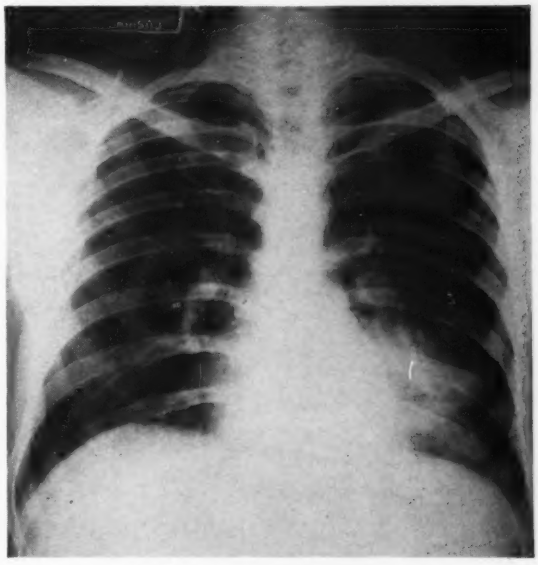

FIG. 1. Case 1. Area of consolidation in left lower lobe containing cavity with a fluid level.

At operation one week later, a large cavity was found in the basal portion of the left lower lobe measuring 8 by 4 by 4 cm. The walls of the cavity measured about 1 cm. in thickness, and the surrounding parenchyma was firm, noncrepitant and gray with cavities up to 1 cm. in diameter scattered throughout. This lobe was removed, and the patient was discharged asymptomatic on August 17, 1950.

Nine days later, the patient was re-admitted because of drenching sweats and fever. Now his blood pressure, which had been 105 mm. Hg systolic and 60 mm. diastolic, was 140 mm. Hg systolic and 80 mm. diastolic. Further,

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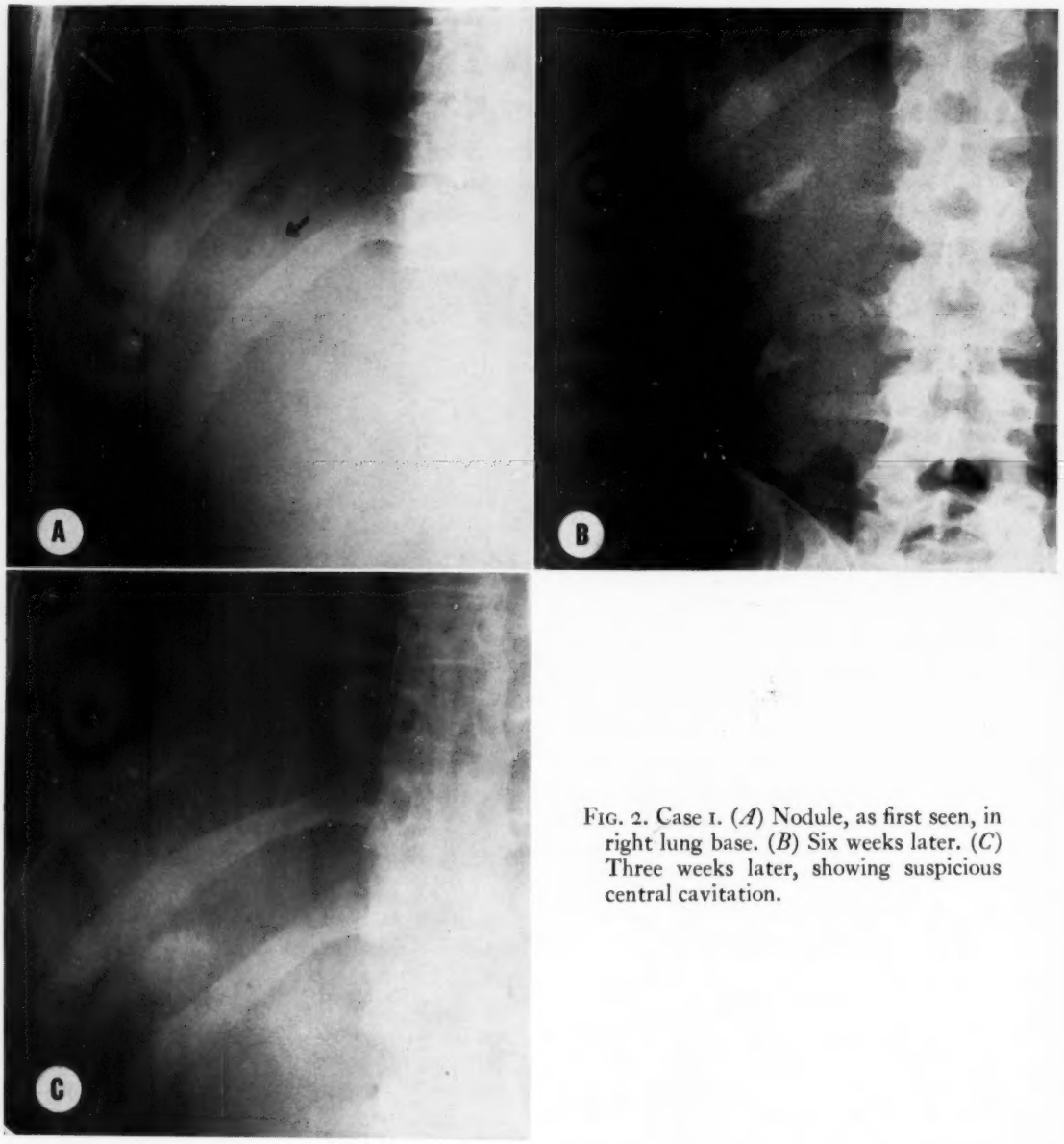

Fig. 2. Case 1. (*A*) Nodule, as first seen, in right lung base. (*B*) Six weeks later. (*C*) Three weeks later, showing suspicious central cavitation.

urinalysis, previously negative, showed a specific gravity ranging from 1.002 to 1.015, a slight trace to 3+ albumin, no sugar, many finely and coarsely granular casts and many red blood cells. The nonprotein nitrogen varied from 27 to 131 mg. per 100 ml. No pathogenic organisms were recovered from the urine, sputum, or feces, and blood cultures were negative. Until the patient died two months later, he complained of aches and pains in the joints, had bloody rectal mucoid discharges, gross hematuria, epistaxis, petechiae, marked conjunctivitis, pustular skin lesions and a progressive ulcerative stomatitis.

During this period, a well circumscribed round patch of consolidation about 2 cm. in diameter in the right lung base was observed through the shadow of the liver (Fig. 2), and this was subsequently demonstrated to lie in the posterior basal segment. Review of previous films revealed the first indication of this lesion on film taken about six weeks earlier, at which time it measured 1 cm. in diameter. In about three weeks the lesion grew to about 3 cm., and

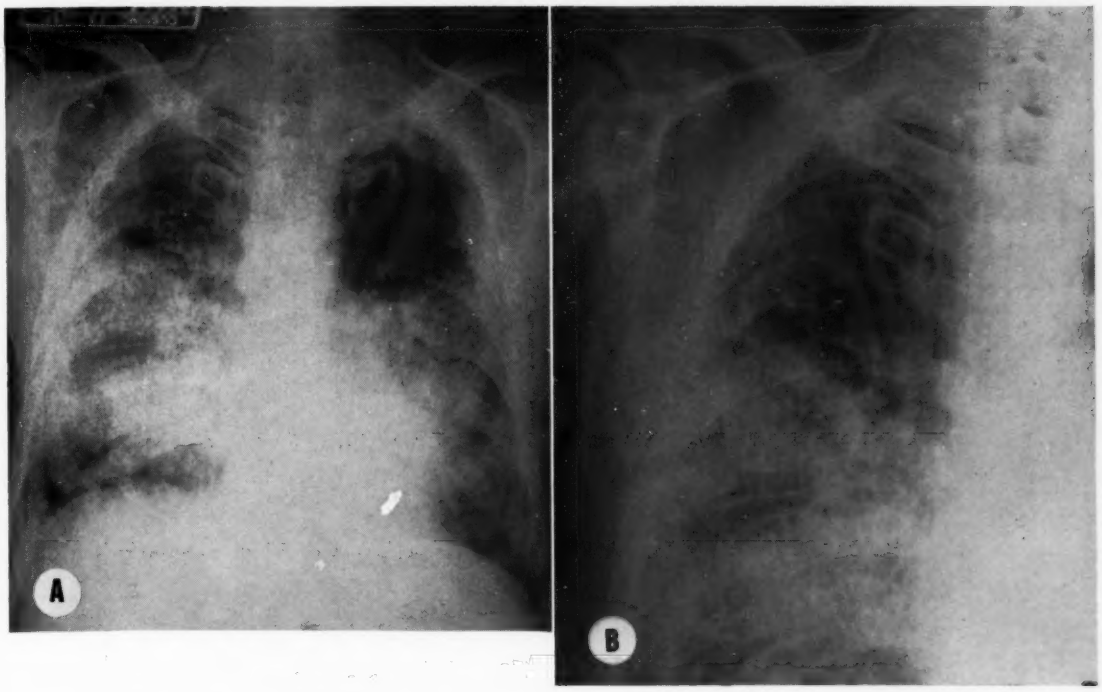

Fig. 3. Case II. (*A*) Diffuse pulmonary nodulation and central densities suggesting edema. (*B*) Detail of right lung.

showed suspicious central cavitations. At autopsy, this nodule and several other smaller pulmonary nodules were found. They were firm, gray, well circumscribed, and some had necrotic centers.

Case II. A fifty year old, severely ill white man was admitted to the hospital October 30, 1950, complaining of shortness of breath and weakness of one month's duration with fever, morning cough productive of nonfoul, gray-white sputum with blood. Occasional joint pains were felt. There was bronchovesicular breathing over both apices, and signs of consolidation were present in both lung bases. Blood sulfonamide level was 1.5 mg. per 100 ml. Urine possessed a specific gravity of 1.010 to 1.015, 1 to 3+ albumin and no sugar; the sediment contained 50 to 80 red blood cells in high power field and many finely and coarsely granular casts. The white blood cell count varied from 10,700 to 35,300 with 1 to 3 per cent eosinophils. Nonprotein nitrogen rose from 74 mg. initially to 154 mg. per 100 ml. two days before death. Smears and cultures of sputum showed no pathogenic organisms. Blood pressure varied from 116 to 100 mm. Hg systolic and 70 to 76 mm. Hg diastolic. Urinary output declined just before death nine days after admission.

Posteroanterior chest film on admission (Fig. 3) showed bilateral pulmonary, diffusely scattered, discrete and confluent nodules, most marked centrally. These nodules were not calcified, and varied in size from a few millimeters to 1 cm. in diameter. Poorly demarcated densities suggesting pulmonary edema were present in the central portions of both lungs obscuring the outlines of the hilar blood vessels. No definite cavitation could be distinguished. The heart was not enlarged, but the arc of the pulmonary artery on the left border was prominent. At autopsy, numerous well circumscribed nodules were present in both lungs similar to those present in the first case, and the parenchyma about these lesions was moderately spongy and moist.

Case III. A thirty-seven year old white male was admitted to the hospital on June 12, 1950, with complaints of hemoptysis two days previously. In 1943 he first experienced hemoptysis and following this, until the present admission, he had periods of night sweats, moderate shortness of breath, wheezing, coughing with small amounts of sputum, fatigue and

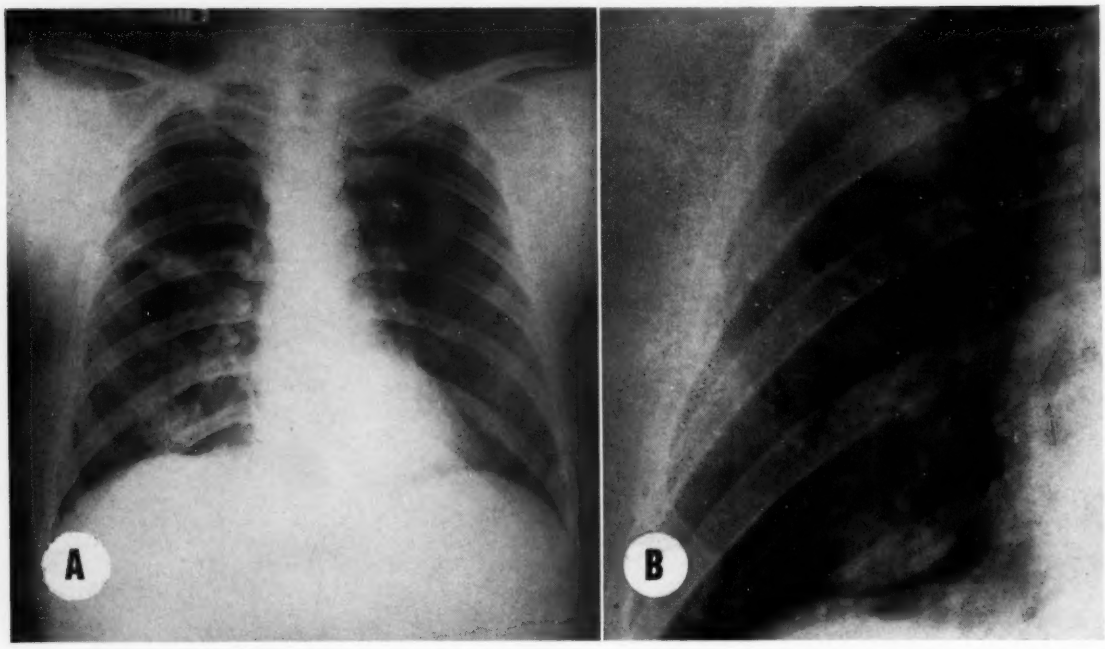

Fig. 4. Case III. (*A*) Mass in anterior segment of right upper lobe, and larger mass in anterior basal segment of right lower lobe. (*B*) Detail of lesions in left oblique view showing faint patchy consolidations in the regions of the masses and focal plate-like atelectatic changes in the vicinity of the upper nodule.

sharp pains in the chest. Occasional hemoptysis was present. For these symptoms he had been hospitalized seven times. He spent a month in a tuberculosis hospital, and sputum examination for acid-fast bacilli and tuberculin tests were negative. Repeated physical examination during this admission revealed coarse inspiratory and expiratory rhonchi, sibilant and sonorous rales and wheezing in the right chest. Breath sounds were diminished over the right upper chest anteriorly and posteriorly. No acid-fast bacilli were found in the sputum during this admission. Bronchoscopic examinations were negative. No abnormality was found in the urine.

Chest roentgenogram dated July 20, 1950 (Fig. 4) showed a fairly well circumscribed mass about 2 cm. in diameter in the anterior segment of the right upper lobe and a similar but somewhat less demarcated mass about 4 cm. in diameter in the anterior basal segment of the right lower lobe. No calcium and no cavitation could be distinguished in these lesions. The parenchyma surrounding both these lesions showed faint patchy consolidations and, in addition, plate-like atelectatic areas were present in the vicinity of the upper lobe lesion. The chest otherwise had a normal appearance, except for a large calcified right paratracheal node. Several chest films since 1947 showed these lesions unchanged.

Right multiple segmental lobectomies were performed on October 7, 1950, and three masses were removed: one in the anterior segment of the right upper lobe and two in the basal segments of the right lower lobe. The upper lobe mass measured 11.5 by 9 by 4 cm., and the other two areas from the lower lobe measured 6 by 4 by 0.2 cm. and 3 by 2 by 2 cm. A noncrepitant, nonfibrotic, meaty, grayish-black parenchyma surrounded each well demarcated mass. The masses were composed of black to grayish-white tissue with small cavities occasionally measuring up to 0.8 cm. in diameter. A segmented bronchus frequently entered the mass. Following operation, the patient continued to have shortness of breath and wheezing. He was last seen in December, 1951, still suffering from asthma.

PATHOLOGICAL FINDINGS

In the lungs of the first 2 cases the masses that were noted grossly consisted of granulomatous tissue with little collagen present. Small foci of necrosis surrounded by

palisaded epithelioid-like cells were numerous in the first case, but rare in the second. In some regions the alveoli were filled with vacuolated macrophages containing abundant cholesterol. Marked ulceration of the bronchioles had occurred with destruction of the walls and occlusion of the lumina. Dilatation of these ulcerated structures led to cavity formation. The walls of scattered arteries and veins were replaced by fibroblasts, histiocytes and eosinophils. Extensive destruction of the elastic laminae was found. Marked coagulative necrosis had occurred in the spleen, with only a thin zone of pliable tissue just below the capsule. In the kidneys of both cases, crescent formation, focal thromboses in the glomeruli and periglomerular granulomas were found. In the first case, one renal artery with features of the healed periarteritis nodosa was found. Homogenous eosinophilic material had replaced the walls of arteries in the gastrointestinal tract of the first case, and only remnants of the elastic laminae remained. Bacteriological studies, including animal inoculation, disclosed no significant organism in both cases.

In the third case large regions of dense acellular fibrotic tissue were present in the lungs. Masses of vacuolated macrophages with cholesterol-rich lipoid were present within the alveoli still remaining at the periphery of the fibrous masses. Many of the bronchioles and small bronchi were dilated and lined by metaplastic stratified squamous epithelium, and some of these structures were ulcerated and necrotic, producing cavities lined by necrotic granulation tissues. The walls of the blood vessels were often disorganized and fibrotic, with extensive fragmentation and disappearance of the elastic lamina. Bacteriological studies were negative.

DISCUSSION

This disease is marked by the formation of aseptic, pulmonary circumscribed granulomatous masses in which cavity formation and necrotizing arteritis and phlebitis may be seen. These cavities are due to ulceration of the bronchioles and small bronchi. The obstruction of these small branches of the bronchial tree, caused by these ulcerations, leads to the accumulation of intra-alveolar vacuolated phagocytes filled with cholesterol. These changes are usually accompanied by splenic necrosis and focal thrombotic granulomatous glomerulonephritis.

Many reports favor hypersensitivity as the causal factor in this disease. In Cases I and II sulfonamide appears to be the probable sensitizing agent. For a discussion of the etiology and the relationship of the entire complex to periarteritis nodosa, the reader is referred to Fienberg's recent communication.[1] The varied interpretations of these lesions which have led to such diagnoses as lupus erythematosus, Loeffler's syndrome and pararheumatic disease are also discussed in this article. As illustrated by Case III, the lesions may be confined to the lungs without other organ involvement. In this case, the marked old vascular destruction and abundant fibrous tissue are interpreted as being part of an obsolescent process. Fienberg[2] has called this condition "idiopneumonic necrotizing granulomatosis," and suggested a relationship to chronic pneumonitis of the cholesterol type.

Hemoptysis is a very common symptom in these cases. Fever, night sweats, joint pains, loss of weight and cough are frequently present. Asthma may be present, and eosinophilia is variable. The course of the disease may be protracted, but with the onset of glomerulonephritis the patient's condition generally deteriorates rapidly, and during this period, as in Case I, there may be hemorrhages from the urinary and gastrointestinal tracts. Blood pressure is usually not much elevated.

Most of the reports in the literature of typical cases contain none, or only brief and vague references to roentgenological changes. However, Sandler, Matthews and Bornstein[3] report a typical case in which the roentgenograms are illustrated and described as showing an 8 cm. multilocular cavity in the lung, and a 2 cm. nodule

which increased in size in three months and developed a cavity. After one month these cavitations increased in size and extensive bilateral infiltrative densities developed. Smith[4] described in his typical case an opacity in the left apex with a small central cavity. The rest of the lung showed faint mottling with individual opacities from 1 to 3 mm. in diameter. No change was observed after two months.

Both these reports illustrate roentgen features in common with those described here. The lung lesions are characteristically nodular. These nodules or masses are generally multiple but, as in Case 1, only one such lesion may be visible at one time. They vary in number from one or two isolated lesions to a diffuse miliary spread, and vary in size from the lower limits of visibility to masses several centimeters in diameter. They are generally round, discrete and fairly well demarcated, but the surrounding parenchymal consolidations may at times obscure their borders, and when these lesions are present in large numbers they may be confluent.

No characteristic localization of these lesions can be determined as yet. They have not exhibited calcific deposits. The necrotizing process in these masses is frequently manifest as visible cavitation, and this is a prominent roentgenological feature. These cavities are variable in size and may be multilocular. The walls may be irregular. The course of these lesions is variable. They may progress fairly rapidly as in Case 1, and as reported by Sanders *et al.*, or they may remain stationary for years, as in Case III. Focal atelectatic changes may be present in the vicinity of these nodules, but lobar contraction has not been noted. In all the cases the heart has not been enlarged. No pleural effusion has been observed roentgenologically.

As far as is known, the diagnosis has never been suggested on the basis of roentgenological findings. The pulmonary lesions themselves do not present any distinguishing diagnostic features. However, with the onset of focal glomerulonephritis, recognition appears possible. A distinctive diagnostic picture is produced when pulmonary nodules with cavities, as described above, are found combined with signs of glomerulonephritis. Other clinical manifestations supporting the diagnosis are the presence of hemoptysis, fever and joint pains, and the absence of marked hypertension and cardiac enlargement.

SUMMARY

The roentgen manifestations of three cases of necrotizing granulomatosis are described as well as the pathological and clinical features. The characteristic roentgenological changes are presented so that they can be of aid in the diagnosis of this disease.

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THE ROENTGENOLOGIC ASPECTS OF CHORDOMA*

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ONE of the few neoplasms which originate from and retain the histologic structure of primitive embryonic tissue is the chordoma. This relatively rare malignant tumor derived from remnants of the notochord is slowly growing and locally invasive, but tends to recur following attempts at surgical removal. Because of the insidious onset the growth may be present for a long period before medical treatment is sought. For this reason complete surgical excision may be difficult and at times impossible. As in all other types of malignant lesions, the objective is earlier diagnosis and commensurate treatment. It is the purpose of this paper to present the clinical manifestations and roentgenographic findings as an aid in effectuating this goal.

REVIEW OF LITERATURE

Embryology. The highest phylum in the animal kingdom, the Chordata, is characterized by a rodlike back support called the "notochord" or "chorda dorsalis."[2] In the amphioxus, a very primitive fishlike form of chordate, the notochord is the only axial skeletal structure;[16] but in the highest group of chordates, the Vertebrata, the notochord is replaced by a bony structure forming the skull and vertebral column.[20] As the mesodermal tissue envelops the notochord and neural tube laying down cartilage, the notochord evolves into a large single sigmoid curve in the midsagittal plane at the base of the skull.[35,37] This carries it into close proximity to the surface of the cartilage at four points. It is near the dorsal surface in the hypophyseal fossa and on the clivus of Blumenbach caudad to the hypophyseal fossa or anterior to the foramen magnum. The notochord is closest to the ventral surface of the developing skull midway between the fossa and foramen magnum where it may involve the pharyngeal epithelium. Ectopic rests of cells may also occur in the mandible or maxilla if fragments become separated from the notochord. It is in one of these four areas near the cartilaginous surface that cranial chordomas originate.

The S-shaped cranial notochord continues caudally into the mesodermal elements which eventually give origin to the vertebral bodies, the sacrum and the coccyx.[24] As the notochordal cells are engulfed in this mass of developing bone, they are either enclosed within it or forced out on the surface.[25] In the vertebral part of the axial skeleton the intravertebral portion of the notochord is extruded between the vertebral bodies and, along with the intervertebral portion, forms the nucleus pulposus of the intervertebral disks. Any remaining vestiges within the vertebral bodies are extremely rare, since the notochordal cells can escape freely. Such is not always the case in the cranial and caudal portions where the notochord is more completely encased within the cartilage. Normally the captured cells degenerate and disappear, but in rare instances they may remain as rests of primitive notochordal cells. It is believed that from these abnormally enclosed vestiges the rare neo-

* Abridgment of thesis submitted by Dr. Utne to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Radiology.

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TABLE I

CASES OF CHORDOMA REPORTED IN THE LITERATURE

Author	Year	Cranial		Vertebral					Sacro-coccygeal		Total Cases
		Total	Per Cent	Cervical	Thoracic	Lumbar	Total	Per Cent	Total	Per Cent	
Coenen[5]	1925	21	45	1			1	2	25	53	47
Mabrey[18]	1935	49	33				14	9	87	58	150
Faust and associates[10]	1944	96	38				34	14	122	48	252
Tonelli[30]	1948	118	37	15	8	19	42	13	157	50	317
Present authors	1954	197	39	37	12	32	81	16	227	45	505

plasm, chordoma, develops. Clusters of chordal cells occurring on the surface apparently are benign in nature and are far commoner than the malignant counterpart developing from the enclosed cells. They are of no clinical significance and have been reported to occur in 2 per cent of all necropsy specimens.[23]

Review of Cases. The first to describe these small jellylike excrescences of tissue was Luschka in 1856.[17] Virchow[33] rendered a more complete account of these protrusions and noted the large vacuolated "physaliphorous" cells which he believed to be of cartilaginous origin. Müller[21] in 1857 discovered the remarkable resemblance of these cells to notochordal tissue and suggested that they be called "chordoid tumors."

By 1895 additional cases had been studied[28] and Ribbert proved by animal experimentation[23] that the hypothesis of notochordal origin of chordomas was correct.

Further examples appeared in the foreign and domestic literature,[29,31] and by 1925 Coenen[5] had collected data on 47 cases of malignant chordoma (Table I). From this group he formulated a classification which, slightly modified, is outlined in Table II. Ten years later Mabrey[18] compiled a series of 150 cases. Faust and associates[10] in 1944 and Tonelli[30] in 1948 gathered the available reports totaling 252 and 317 respectively. A review of subsequent publications[31] in addition to the examples herein reported reveals a total of 505 cases cited in the literature.

MATERIAL AND METHODS

The subject matter included in this study comprised an analysis of the clinical manifestations in 72 cases of histologically proved chordoma found in the files of the Mayo Clinic from 1910 through 1953. Original roentgenograms unaltered by previous treatment were examined in 41 cases. Thirteen of the cases have not been reported previously. Prior articles include pathologic studies by Fletcher,[11] Fletcher and associates[12] and Dahlin and MacCarty,[7] and surgical results by Adson and associates,[1] Whittaker and Pemberton[34] and MacCarty and associates.[19]

DISTRIBUTION AND ETIOLOGIC FACTORS

The locations of the 72 cases of chordoma along the axial skeleton are given in Table II. The cranial group consisted of 18 cases or 25 per cent of the total which was further subdivided into hypophyseal, 5 cases, spheno-occipital, 9 cases, and nasopharyngeal, 4 cases. None was found in the dental group. Vertebral chordomas comprising 19 per cent of the total were located predominantly in the cervical region. The rarity of this neoplasm in the thoracic and lumbar segments of the spinal column was emphasized by this study. A definite predilection for the sacrum and coccyx was

TABLE II

DISTRIBUTION AND ETIOLOGIC FACTORS IN 72 CASES OF CHORDOMA

Classification	Cases	Per Cent of Class	Total Cases	Per Cent of Total	Sex				Age, yr.			Trauma			
					Female	Per Cent	Male	Per Cent	Overall	Female	Male	Female	Male	Total Per Cent	Years
Cranial			18	25	10	56	8	44	37.5	32.4	43.9	2	3	28	9.5
Hypophyseal	5	28													
Spheno-occipital	9	50													
Nasopharyngeal	4	22													
Dental	0	0													
Vertebral			14	19	5	36	9	64	48	48.8	47.4	3	1	29	15.2
Cervical	10	72													
Thoracic	2	14													
Lumbar	2	14													
Sacrococcygeal			40	56	8	20	32	80	50.6	57	48.9	1	19	50	8.5
Antesacral	25	63													
Central	13	32													
Retrosacral	2	5													
Total	72		72	100	23	32	49	68	46.8	44.5	47.8	6	23	40	9.6

shown by the high incidence of 56 per cent in these areas.

When comparing the locations of affected areas in Tables I and II, the distribution of chordomas is approximately one-half sacrococcygeal, one-third cranial, and one-sixth vertebral. It is significant to note that 84 per cent of the cases occurred at the extremes of the axial skeleton. The vertebral portion which has the largest accumulation of persistent notochordal tissue, namely the nuclei pulposi of the intervertebral disks, is also the area least affected by tumors of notochordal origin.[14] This would suggest that the tumor does not arise from notochordal cells in their normal location but only from those cells which are ectopically placed.

As in other types of malignant diseases the actual cause of chordomas has not been determined; however, certain predisposing factors might contribute to their development. The significance of eliciting a history of previous trauma to the affected area is of questionable value in determining the etiology of a neoplasm,[13] but some interesting facts to support the view were obtained from the study. Injury to the lower back probably occurs more commonly in men than in women; but as the cranium is approached, trauma is less likely to predominate in either sex. Accordingly the variations in the ratio of females to males in the sacrococcygeal, vertebral and cranial regions as given in Table II were approximately 1:4, 1:2 and 1:1. Distribution of the tumor also suggests a relationship with trauma. Since low back injuries are more frequent than head and neck injuries, the sacrococcygeal area comprised as many cases as the other two areas combined. A history of previous trauma, frequently severe enough to require medical attention, was given by 40 per cent of the total number of patients. One-half of the sacral patients had a positive history of injury of which a remarkably high (95) per cent were males. A correlation of the high incidence of previous injury, the distribution and the male sexual preponderance might suggest that trauma does play a significant role as a predisposing factor to the development of a chordoma. It has been postulated that trauma causes a release of chordal cells from within their fibrous capsule or that it stimulates neoplasia in heterotopic rests of chordal cells,[3] but it is generally accepted that a malignant lesion does not arise from notochordal cells situated in their normal location.[6]

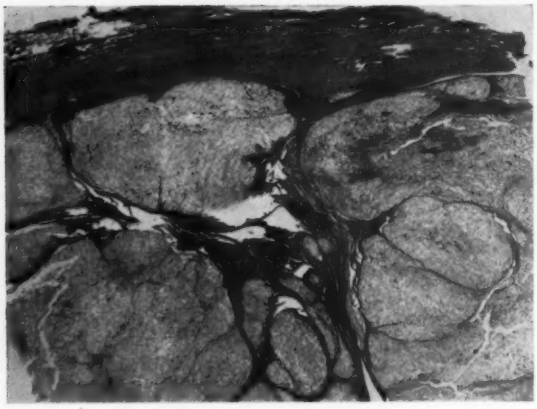

Fig. 1. Cellular pattern of a chordoma, demonstrating the arrangement in lobules of varying size separated by fibrous septa. A well-defined capsule surrounds the irregular tumor mass (hematoxylin and eosin).

The age incidence of the patients at the time of admission to the clinic ranged from eight to seventy-six years with a mean of 46.8 years as seen in Table II. Intracranial tumors gave rise to symptoms thirteen years earlier than the sacrococcygeal tumors. This was explained by the fact that even a small cranial mass confined within a limited space will encroach on adjacent structures, producing symptoms earlier than an unrestricted pelvic tumor.

Skeletal congenital anomalies of the lower back, found in 4 of the 40 sacrococcygeal cases, were not considered to be significantly associated with the tumor arising from embryonic tissue.

PATHOLOGY

Gross Pathology. The morbid anatomic pattern of the chordomas bore a striking resemblance to their parent tissue, the notochord. The tumors consisted of lobules of gelatinous or mucoid tissue surrounded by fibrous septa and enclosed within a well-defined capsule as demonstrated in Figure 1.

The tumor mass varied in size from small to very large, the largest measuring 42 by 13 by 12 cm. and weighing 4,200 gm. Cystic degeneration and hemorrhage into the lobules gave a "currant-jelly" appearance. Osseous sequestra of engulfed bone or fragments of dystrophic calcification were frequently scattered throughout the slowly growing neoplasm.

Microscopic Pathology. The salient features of the histopathology included:

1. Cellular Pattern. Within the lobules, the cells were arranged in cords or strands lying perpendicular to the fibrous septa (Fig. 2).

2. Cellular Structure. Intracellular mucin forming cytoplasmic vacuoles was found in some portion of the tumor in every case. The very large intracellular vacuoles producing physaliphorous cells as seen in Figure 3 were prominent in one-half of the cases. Characteristics indicative of a malignant tumor were found in one-third of the microscopic sections.

3. Extracellular Mucin. A varying amount of mucus forming a background outside the cells was found in every case. At times the cell boundaries were completely lost and the appearance was that of a syncytium with nuclei lying in a sea of mucus.

It was amply demonstrated that a wide variation of appearances may be noted in different areas of the same tumor and it is therefore recommended that sections be selected and studied from numerous por-

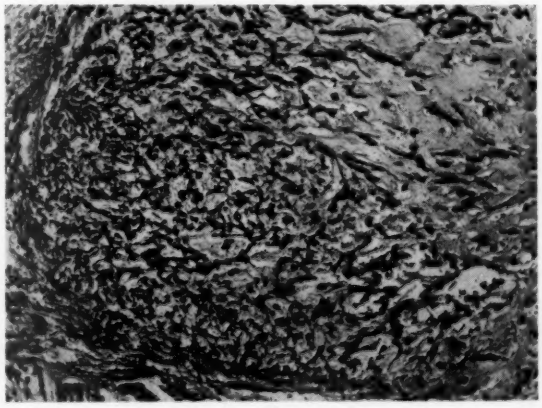

Fig. 2. Arrangement of the cells in cords and strands lying perpendicular to the fibrous septa. The cells are more numerous at the periphery near the septa, and extracellular mucin predominates at the center of the lobule (upper right corner) (hematoxylin and eosin).

Table III

PRESENTING COMPLAINTS IN 18 CASES OF CRANIAL CHORDOMA

	Number	Per Cent	Duration mo.
1. *Increased intracranial pressure*			
a. Headache	13	72	12.9
b. Vomiting	5	28	6.9
c. Ocular disturbances	12	67	
1. Subjective (diplopia, blurring)	9	50	22.6
2. Objective (choked disk, optic atrophy)	4	22	
d. General signs and symptoms (lethargy, fatigue, weakness, emotional instability, depression, flight of ideas, forgetfulness)	10	56	16.3
2. *Pressure on adjacent structures*			
a. Hypophyseal			
1. Disturbed endocrine function	4	22	20.4
2. Abnormal visual fields	6	33	
b. Spheno-occipital			
1. Cranial nerve involvement	15	83	7.9
2. Cerebral involvement (hemiparesis)	1	6	2
3. Cerebellar involvement (ataxia)	3	17	2
4. Cerebellopontine angle (deafness, dizziness, tinnitus)	3	17	
c. Nasopharyngeal			
1. Obstructed breathing	4	22	5.8
2. Nasal discharge	1	6	
3. Pain	2	11	
4. Palpable mass	3	17	
d. Dental	0	0	

tions of each tumor.

A metastasis was proved in only 1 instance. The spread from a sacrococcygeal chordoma in a forty-two year old man was to the scapula. The clinical course in 2 other patients suggested a metastatic lesion, but no confirmation was obtained.

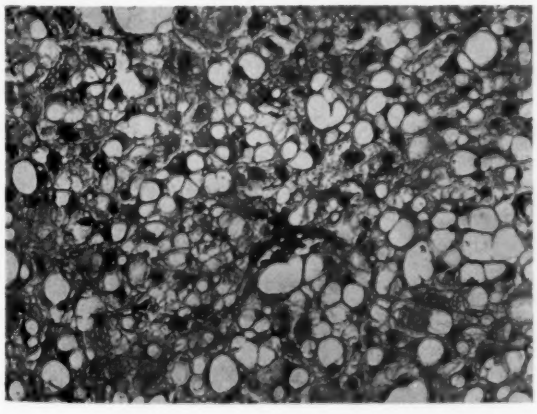

Fig. 3. Large, intracellular vacuoles of mucin characteristic of the physaliphorous cells. Nuclear vacuoles also are present (hematoxylin and eosin).

SYMPTOMATOLOGY

The presenting complaints and physical findings varied according to the location and direction of spread, but in all areas the findings were due to the presence of a slowly expanding tumor mass.

A. *Cranial.* The symptoms of the 18 cranial chordomas resulted from a slowly expanding tumor at the base of the brain usually originating near the midline. This space-occupying mass caused increased intracranial pressure or encroachment on adjacent structures (Table III).

1. Increased Intracranial Pressure. The pressure symptoms were not specific for a chordoma but usually were the first disturbance noted by the patient.

a. Headache, the most frequent complaint, occurred early in the disease. Locali-

TABLE IV

PRESENTING COMPLAINTS IN 14 CASES OF VERTEBRAL CHORDOMA

	Number	Per Cent	Duration, mo.
1. *Effect on adjacent extravertebral structures*			
a. Esophagus (dysphagia)	3	21	5.8
b. Trachea (difficult breathing, hoarseness)	3	21	2.4
c. Paravertebral muscles (stiffness, pain)	1	7	
2. *Effect on spinal cord or emerging nerves*			
a. Sensory			
1. Pain	10	17	14
2. Numbness	10	71	26.8
3. Paresthesia	2	14	5
4. Proprioceptive	3	21	2
b. Motor			
1. Power (weakness, paralysis)	6	43	31.4
2. Tone (flaccid or spastic)	1	7	
3. Atrophy	2	14	
4. Abnormal reflexes	3	21	
5. Incontinence (feces or urine)	2	14	4.5
3. *Palpable mass*	6	43	11.3

zation to one area was not uncommon.

b. Vomiting associated with the headaches usually was a later complaint.

c. Ocular disturbances present as an early finding in two-thirds of the patients included subjective complaints of diplopia or blurred vision and objective ocular disturbances of choked disk or optic atrophy.

d. General signs and symptoms comprised a varied group of complaints and changes in personality as seen in Table III.

2. Pressure on Adjacent Structures. The structures involved depended on the site of origin of the tumor in one of the four anatomic areas as previously described.

a. Hypophyseal. Chordomas arising in the hypophyseal region were indistinguishable from other parasellar, prechiasmal or pituitary tumors. Disturbances of endocrine function on the basis of pituitary insufficiency included amenorrhea, sterility, loss of libido and marked gain of weight. Abnormal visual fields found in 6 patients ranged from the bitemporal hemianopsia of an optic chiasmal lesion to total blindness.

b. Spheno-occipital. Early symptoms of chordomas involving the clivus of Blumenbach were those of a midline tumor near the brain stem but, as extension occurred, lateral structures were affected. The most frequent physical findings was involvement of the cranial nerves, usually of relatively short duration. Each of the 12 pairs of cranial nerves was involved in at least 1 case as a result of extension into the anterior, middle or posterior cranial fossae. An abducens nerve palsy leading to weakness of the lateral rectus muscle and diplopia was present in one-half of the cranial cases. The involvement of the cranial nerves tended to be unilateral early in the course of the disease. A typical picture was that of multiple, consecutive nerves being affected on only one side. The cranial nerve palsy was due either to direct pressure on the nerve fibers or to stretching of the nerve as the tumor lifted the brain away from the base of the skull.

Symptoms of extension of the tumor into the surrounding brain tissue were uncommon and of short duration. Lateral extension with symptoms of a cerebellopontine angle tumor was seen in 3 cases.

Table V

PRESENTING COMPLAINTS IN 40 CASES OF SACROCOCCYGEAL CHORDOMA

	Number	Per Cent	Duration, mo.
1. *Effect on adjacent extravertebral structures*			
a. Intestinal tract			
1. Constipation	29	72	13.9
2. Rectal bleeding	2	5	3.5
b. Urinary tract			
1. Difficulty in starting urination	5	12	1.9
2. Dysuria	3	8	14.3
3. Frequency and urgency	3	8	7.0
2. *Effect on emerging nerves*			
a. Sensory			
1. Pain	38	95	34.6
2. Numbness	8	20	10
3. Paresthesia	1	2	4
4. Proprioceptive	0	0	
b. Motor			
1. Power (weakness, paralysis)	1	2	0.5
2. Tone (flaccid, spastic)	0	0	
3. Atrophy	1	2	
4. Abnormal reflexes	3	8	
5. Incontinence (feces or urine)	5	12	28.8
3. *Palpable mass*			
a. Internal	34	85	
b. External	11	28	21.4

c. Nasopharyngeal. The presenting complaints in 4 of the 18 cranial chordomas were primarily those of a nasopharyngeal tumor. In 2 additional cases the nasopharynx and sphenoid sinus were secondarily invaded as a late complication. Biopsy of the tumor tissue in these more accessible locations confirmed the diagnosis without further exploration in 4 cases. All of the patients in this group complained of obstructed breathing for relatively short periods averaging less than 6 months. One had a purulent nasal discharge and 2 complained of localized pain. A firm postpharyngeal or palatine mass was palpable in 3 of the patients.

d. Dental. No case of a chordoma involving either the maxilla or the mandible was found in the files of the Mayo Clinic.

B. *Vertebral.* The clinical manifestations of the 14 vertebral chordomas were the result of a slowly growing tumor mass causing pressure on adjacent extravertebral structures or on the spinal cord and emerging nerves (Table IV).

1. Effect on Extravertebral Structures. In the cervical region, when the bulk of the tumor presented anteriorly, pressure on the tubular organs in the neck caused a disturbance of their function such as dysphagia or difficult breathing. Symptoms of anterior extension were not prominent in the thoracic and lumbar groups.

2. Effect on Spinal Cord or Emerging Nerves. Lateral or posterior extension of the expanding neoplasm caused impingement on the spinal cord or emerging nerves, resulting in presenting complaints of sensory and motor dysfunction.

a. Sensory. The earliest complaint in most of the patients, averaging more than two years in duration, was numbness affecting either one arm or one leg. This was usually followed by pain which was referred

along the course of the spinal nerve. Paresthesia and loss of proprioceptive sensory function were of short duration or late complications.

b. Motor. A loss of muscle power ranging from mild paresis to complete paralysis of one extremity was present in 6 cases for an average duration of thirty-one months prior to admission. Paraplegia or quadriplegia was found in 2 cases but only as a late complication. Other disturbances of motor function, as seen in spinal cord tumors, were usually of short duration.

3. Palpable Mass. The presence of a tumor in the neck was noted by 6 patients, averaging about one year before admission for treatment. The tumors ranged in size from 5 to 8 cm. and were associated with the symptoms of compression of the esophagus or trachea.

C. *Sacrococcygeal.* The 40 sacrococcygeal chordomas produced symptoms due to pressure on the adjacent extravertebral structures or on the emerging nerves as outlined in Table v.

1. Effect on Adjacent Extravertebral Structures. The two organ systems most frequently involved were the intestinal and urinary tracts. Constipation was a prominent feature in about three-fourths of the cases. Rectal bleeding, however, was uncommon and proctoscopic examination failed to show mucosal involvement in any of the cases.

Presenting complaints on admission referable to the lower urinary tract, such as difficulty in starting urination, dysuria, frequency and urgency, were not severe. Late in the course of the disease vesical dysfunction often became a prominent symptom as a result either of direct pressure from the mass or of a neurogenic "cord bladder."

2. Effect on Emerging Nerves. Involvement of the sacral, pudendal or coccygeal nerves resulted in sensory or motor disturbances in nearly every patient.

a. Sensory. Pain was the most frequent and earliest complaint, occurring in 95 per cent of the patients for an average of nearly three years prior to admission. In 2 instances pain of gradually increasing severity had been present for eighteen years. The pain was usually mild and localized to "the end of the spine" or in the rectum early in the disease. As the disease progressed, the pain became intense and intractable with radiation along the sciatic nerves. A diagnosis of hemorrhoids treated surgically without relief was part of the history of 14 patients.

Numbness occurring in 20 per cent of the patients was less prominent than in the vertebral region. The decreased sensation was localized to the perianal area and followed long after the pain had been present. Paresthesias were not prominent and proprioceptive disturbances were absent at this low level beyond the end of the spinal cord.

b. Motor. Disturbances of muscle function were far less prevalent in the sacrococcygeal area than in any other region. Only 5 per cent of the patients showed evidence of weakness or muscular atrophy. When the sacral nerves were affected in advanced cases fecal and urinary incontinence occurred.

3. Palpable Mass. The presence of an external tumor growing near the end of the spinal column was noted by 11 of the patients and had been present for an average of 21.4 months. In addition, at the time of admission, a presacral mass could be palpated in 34 of the patients. Typically the tumor was described as being round, smooth, firm, and occasionally cystic. It was located retrorectally near the midline in the hollow of the sacrum.

ROENTGENOGRAPHIC FINDINGS

The roentgenographic findings, regardless of the location of the chordoma, were based on the presence of bone involvement and a soft tissue mass (Table vi). Some degree of bony change was evident in 83 per cent of the cases in this series, and in other published reports it has been found in every case.[13] The presence of a soft tissue mass was found in 80 per cent of the cases either

TABLE VI

ROENTGENOGRAPHIC FINDINGS IN CHORDOMA

Location	Cases	Bone Involvement	Number*	Per Cent Positive	Soft Tissue Mass	Number†	Per Cent Positive
Cranial	13	1. Clivus	8	62	1. Direct evidence	2	15
		2. Sella turcica	9	69	2. Indirect evidence		
		3. Sphenoid bone	1	8	a. Air studies (3 cases)	3	100
		4. Petrous bone	2	15	b. Angiograms (3 cases)	1	33
					c. Calcification	2	15
					d. Displaced pineal	2	15
		Total	12	92	Total	8	62
Vertebral	8	1. Vertebral destruction	6	75	1. Direct evidence	7	88
		2. Pathologic fracture	2	25	2. Indirect evidence		
		3. Increased density	4	50	a. Trachea displaced (6 cervical)	5	83
		4. Intervertebral disk involved	2	25	b. Aorta displaced	1	12
					c. Calcification	5	62
					d. Myelography	0	0
		Total	7	88	Total	8	100
Sacrococcygeal	20	1. Sacral destruction	15	75	1. Direct evidence	17	85
		2. Scalloped margin	11	55	2. Indirect evidence		
		3. Trabeculation	9	45	a. Displaced rectum	2	10
		4. Expansion	10	50	b. Calcification	10	50
		Total	15	75	Total	17	85

* There may be more than one type of bone involvement in the same case.
† There may be more than one type of evidence of a soft tissue mass in the same case.

by direct visualization of the tumor shadow or by indirect evidence.

A. *Cranial.* The most helpful procedure in revealing the presence and location of a cranial chordoma was roentgenographic examination. Positive findings were present for each of the 13 cases in which films were available. Bone involvement was present in all but 1 case and direct or indirect evidence of a soft tissue mass was found in 8.

1. Bone Involvement. There were no distinguishing features about the bone destruction but the typical location in which it occurred was indicative of a midline tumor at the base of the skull. The osteolytic process was due to erosion from the slowly expanding tumor or actual invasion and malignant destruction. The spheno-occipital and hypophyseal areas were the commonest sites of origin, and therefore these structures were most frequently involved. Some portion of the sella turcica was affected in 69 per cent of the cases. The dorsum sellae was usually destroyed first, with the posterior clinoid processes, the hypophyseal floor and the anterior clinoid processes affected later, as illustrated in Figure 4.

Destruction of the clivus of Blumenbach was found in 62 per cent. The basal skull view seen in Figure 5 was particularly helpful in demonstrating the degree of involvement of the clivus. No consistent type of defect was noted throughout the films studied.[27,32]

Invasion with destruction of the sphenoid and petrous bones was noted in 3 cases.

2. Soft Tissue Mass. Visualization of the outline of the tumor provided direct evidence of the cranial neoplasm in 2 patients. Extension of the growth into the nasopharynx resulted in a contrasting shadow between the tumor and air in 1 case. Figure 6 demonstrates the usefulness of laminagraphy in determining the extent of the soft tissue mass in the other.

The most helpful indirect method of demonstrating the intracranial neoplasm

Fig. 4. Marked sellar enlargement due to destruction of bone of the hypophyseal fossa. Some portion of the sella turcica was involved in 69 per cent of the cranial cases. (From Dahlin, David C., and MacCarty, Collin S. Chordoma: A study of fifty-nine cases. *Cancer* [Nov.] 1952, *5*, 1170–1178, by permission of American Cancer Society, Inc.)

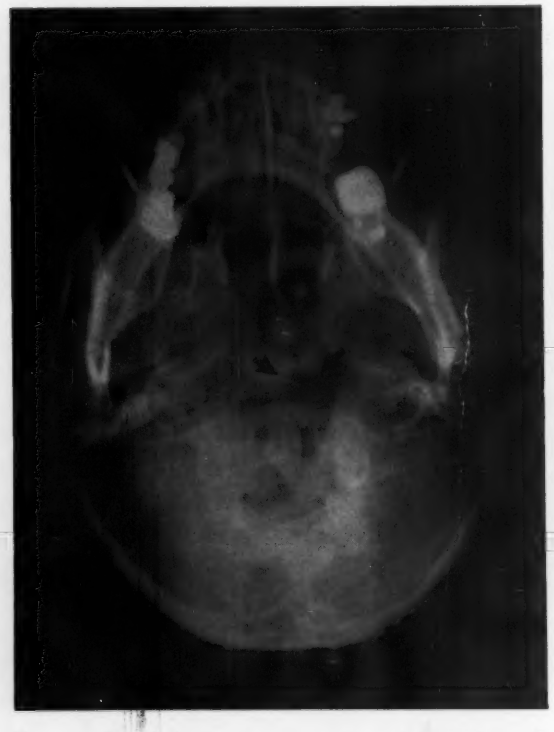

Fig. 5. Basal-skull view revealing destruction of bone of the clivus of Blumenbach due to a sphenooccipital cranial chordoma.

Fig. 6. Lateral laminagram of the skull which directly outlines the soft tissue tumor shadow produced by a hypophyseal cranial chordoma.

was ventriculography. The presence of the midline tumor at the base of the brain was shown by symmetrical dilatation of the lateral and third ventricles, a filling defect

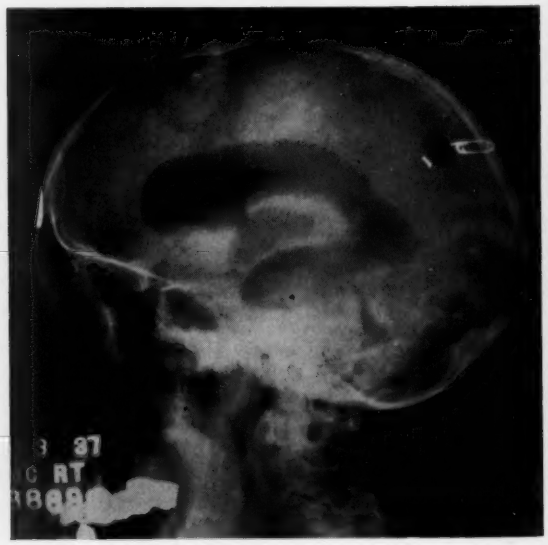

Fig. 7. Ventriculogram of a cranial chordoma indicative of a midline tumor at the base of the brain. There is symmetrical dilatation of the lateral and third ventricles with a filling defect of the floor of the third ventricle. The aqueduct of Sylvius and fourth ventricle are displaced posteriorly.

of the floor of the third ventricle, and posterior displacement of the aqueduct of Sylvius and fourth ventricle. These abnormalities, as shown in Figure 7, were a constant finding in each of the cases in which the procedure was employed.

Cerebral angiography seen in Figure 8 was of diagnostic significance in 1 case. The internal carotid artery was displaced anteriorly, compressed and narrowed by a midline tumor near the base of the skull. Tumor circulation was not seen.

The fact that areas of increased density were found within the tumor mass in only 15 per cent of the cases tended to confirm the view of other writers[4,36] that this feature is not frequently of diagnostic importance. Figure 9 shows a bony sequestrum, verified by tissue examination, which was displaced out of the clivus and carried along within the expanding intracranial malignant lesion. Scattered calcified particles formed in degenerated areas of the neoplasm are illustrated by the view of a necropsy specimen in Figure 10.

Displacement of a calcified pineal gland due to the space-occupying mass was seen in 2 cases.

The clinical and roentgenologic manifestations of cranial chordomas were found to be numerous and varied. Frequently they simulated those of other tumors which are relatively more common. The correct diagnosis was made prior to tissue examination on roentgenographic evidence in only 1 case. However, a chordoma should be considered in the differential diagnosis of any intracranial tumor located in the midline at the base of the brain or in the posterior nasopharynx.

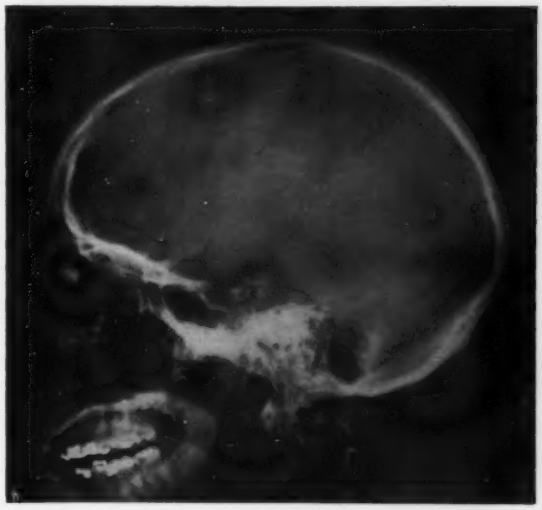

FIG. 9. Spheno-occipital cranial chordoma resulting in destruction of a portion of the clivus and displacement of bony fragments which are being carried along within the expanding intracranial tumor.

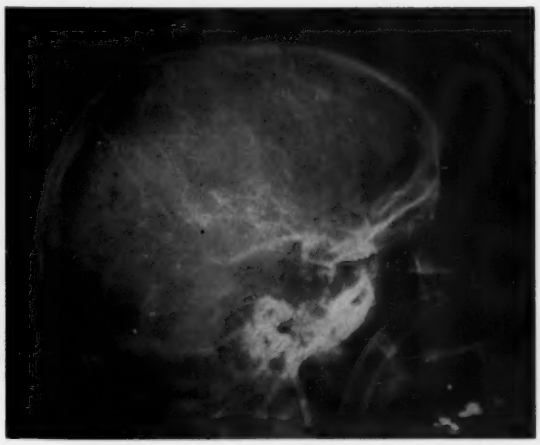

FIG. 8. Cerebral angiogram which demonstrates anterior displacement, compression and narrowing of the internal carotid artery lateral to the sella turcica due to a midline tumor at the base of the brain.

B. *Vertebral.* Roentgenograms of 6 cervical, 1 thoracic and 1 lumbar chordoma showed some abnormality present in each instance. Evidence of bone involvement

FIG. 10. Roentgenogram of a necropsy specimen from a spheno-occipital cranial chordoma. There is scattered calcification within the tumor mass.

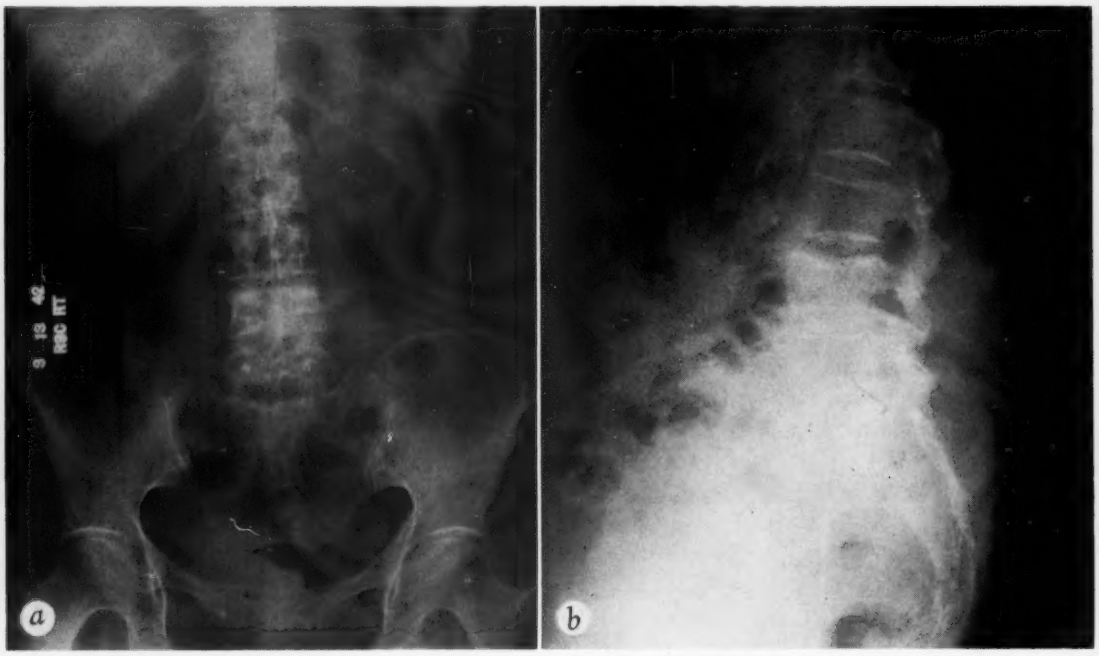

Fig. 11. Anteroposterior (*a*) and lateral (*b*) roentgenograms of a vertebral chordoma affecting the fourth lumbar vertebra. Note the slight compression and apparent expansion of the vertebral body with increased bone density. The calcified abdominal aorta is displaced anteriorly by the soft tissue tumor.

was seen in 88 per cent and a soft tissue mass was found in 100 per cent of the cases studied (Table VI).

1. Bone Involvement. Destruction of some portion of the vertebra was a prominent feature in 75 per cent of the patients. The osteolytic process began in the vertebral body and in half of the cases extended to involve three or more adjacent vertebrae.[9] Pathologic fracture with collapse was found only in the lower thoracic and lumbar regions where weight bearing was more excessive than in the cervical and upper thoracic regions.

An osteoblastic reaction has been reported in the vertebral region by some authors,[8,22] while others maintain that this does not occur in chordomas. The increased density illustrated in Figure 11 was seen in 50 per cent of the cases in this study but was usually associated with compression of bone or rather marked osteoarthritis. The radiodensity could therefore be explained on the basis of these complications or incidental findings rather than new bone formation. Narrowing of the intervertebral disk space also was associated with hypertrophic changes of the vertebral bodies and probably not due to neoplastic invasion.[26]

2. Soft Tissue Mass. Direct evidence of the tumor outline was present in each of the 6 cervical chordomas, as demonstrated in Figure 12. The thoracic chordoma could also be seen on plain films as a soft tissue mass. Laminagraphy was a useful adjunct in determining the extent of the growth and its effect on adjacent structures (Fig. 13). Supplementary evidence of a tumor was provided by displacement of the trachea or aorta, and by the presence of dystrophic calcification or bony sequestra within the neoplasm.

Because the plain roentgenograms adequately revealed an abnormality, it was not necessary in this series of cases to make use of contrast myelography.

The rare vertebral chordomas presented no pathognomonic characteristics which would differentiate them from other tumors near the spinal column. The clinical course

closely resembled that of other more prevalent spinal cord tumors, and therefore a specific diagnosis of chordoma was not made in this region prior to operation.

C. *Sacrococcygeal.* Roentgenograms of 20 cases unaltered by previous treatment revealed positive evidence of a pathologic process in 85 per cent. Bone involvement was found in 75 per cent and direct evidence of a soft tissue mass in 85 per cent of the cases studied as outlined in Table VI.

1. Bone Involvement. Typically the area of destruction which was seen in 15 cases began in the midline and involved the fourth and fifth sacral segments. As the tumor extended, the entire coccyx and wings of the sacrum were eroded. The bone of the sacrum contiguous to the tumor showed irregular scalloped margins (Fig. 14). As the neoplasm invaded or destroyed the osseous tissue, the finer trabeculae were absorbed first; the remaining wider ones produced the findings of coarse trabeculation[15] which was evident in 9 cases.

The encapsulated slowly growing tumor often tended to push and to invade the surrounding structures, resulting in expansion of the cortex of the sacrum. This widening of the diameter of the bone, especially in the anteroposterior plane, was demonstrated in 50 per cent of the cases.

FIG. 13. Anteroposterior laminagram of the neck demonstrating the soft tissue mass and the degree of displacement of the trachea.

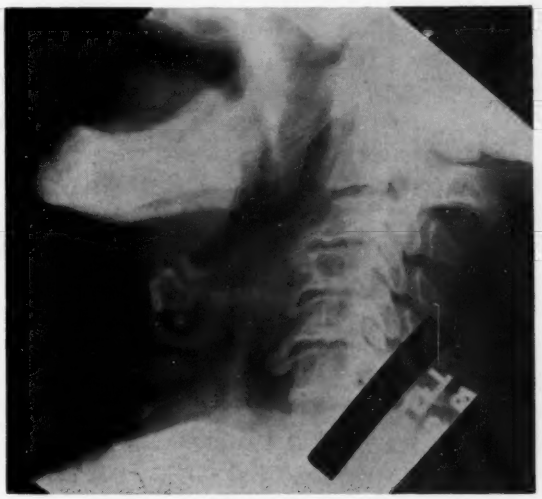

FIG. 12. Lateral view of cervical segment of spinal column demonstrating the soft tissue shadow of a cervical chordoma with extension anterior to the third, fourth and fifth cervical vertebrae. Direct evidence of the tumor mass was present in all of the cervical cases.

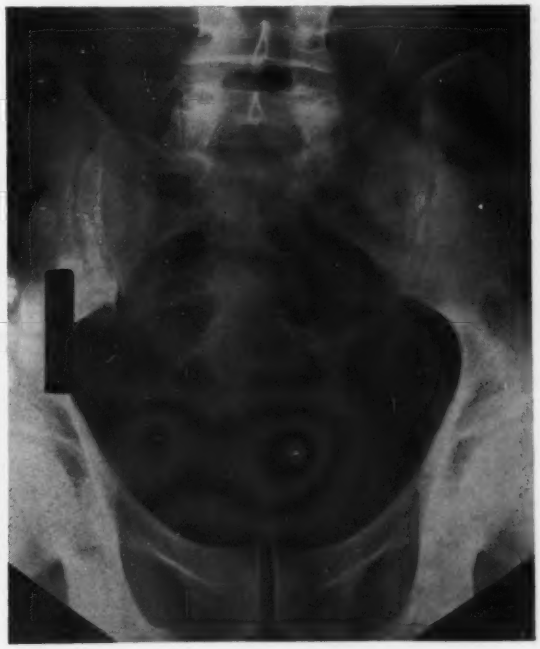

FIG. 14. Anteroposterior roentgenogram of the sacrum which demonstrates the smoothly irregular destruction of the sacrum contiguous to the huge soft tissue tumor filling the pelvis.

Fig. 15. Lateral roentgenogram of a surgically removed sacrococcygeal chordoma. There is destruction and expansion of the sacral cortex with an antesacral soft tissue tumor mass.

2. Soft Tissue Mass. Determination of the size of the tumor by direct visualization of its shadow was possible in 85 per cent of the patients. The mass was predominantly antesacral in most of the cases and extended well beyond the area of destruction of bone as shown in Figure 15.

Indirect evidence of displacement of the rectum by a mass was not of diagnostic importance.

Increased densities within the tumor were prominent in 50 per cent of the cases. An amorphous mass of calcification produced within a necrotic and degenerating tumor was the most frequent finding. The neoplasm also would completely engulf fragments of bone and carry them along as sequestra within the expanding tumor.

The prolonged clinical course and implicative roentgenographic appearances typical of sacrococcygeal chordomas allowed the correct preoperative diagnosis to be made in 40 per cent of the cases studied. It is believed that if one is mindful of the prevalence of this type of malignant neoplasm, and the roentgenographic findings are correlated with the clinical manifestations, a preoperative diagnosis of chordoma can be made in a significantly large percentage of the cases.

SUMMARY AND CONCLUSIONS

1. Chordoma, a slowly growing, malignant tumor arising from vestiges of the embryonic notochord, is not so rare as commonly supposed; reports of more than 500 cases have appeared in the literature.

2. A correlation of the high incidence of previous injury, the distributions of the lesions and the male sexual preponderance suggest that trauma might play a significant role as a predisposing factor to the development of a chordoma.

3. Gross examination of the tumor reveals a round, irregular, encapsulated mass composed of gelatinous or mucoid tissue in lobules which are separated by fibrous septa. The microscopic picture shows the large physaliphorous cells with the typical arrangement in cords or strands lying in a sea of mucus.

4. The similarity of the clinical and roentgenographic manifestations of cranial chordomas to other intracranial neoplasms precludes a correct preoperative diagnosis in most cases, but a chordoma should be considered in the differential diagnosis of all midline tumors at the base of the brain.

5. The presenting complaints and roentgenographic findings of vertebral chordomas reveal no distinguishing characteristics to differentiate them from other tumors of the spinal column.

6. The correct preoperative diagnosis is possible in nearly half of the cases of

sacrococcygeal chordoma. This is based on a correlation of the prolonged clinical course and rather typical roentgenographic manifestations.

7. Roentgenographic examination of a chordoma reveals evidence of bone involvement or a soft tissue mass is more than 90 per cent of the cases.

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STERNAL METASTASES AND THEIR MECHANISM OF PRODUCTION*

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WHILE the regional character of the dissemination makes it easy to follow the spread of metastases by a superficial or deep lymphatic pathway, the route of hematogenous dissemination is always more obscure and difficult to follow, and often is lost without a trace from the moment the neoplastic cells leave the tumor and enter the stream of circulating blood. Recognition and identification of the disseminated portion of the tumor in the blood or in the organs, its later life history, its period of latency and incubation, and its final development require not only great clinical judgment but also, and more often, the use of special techniques and methods of investigation.

As concerns osseous metastases, the various authors who have studied this problem have shown marked preference for the statistical aspects of the contamination, that is with reference to the number and kind of bones affected, and to the extent and type of the metastases observed, rather than to the mechanism or mechanisms of production.

Batson in 1940 described the anatomic aspects of the prevertebral venous plexus which provides a direct communication by hematogenous route between the venous plexuses of the organs of the pelvis and the lower spine and the remainder of the vertebral column and the cranium.

Some of the veins as they leave the numerous venous plexuses of the pelvis flow into this prevertebral venous network, and are potential carriers of neoplastic cells from pelvic tumors, thus explaining the spread of tumors of the prostate, urinary bladder, uterus, ovaries and rectum to the bones of the pelvis, the vertebral column and the cranium.

Walther, in 1945, on the basis of autopsy studies, pointed out four different types of hematogenous neoplastic dissemination, which he designated as follows:

1. Pulmonary type
2. Hepatic type
3. Caval type (Hohlvenentypus)
4. A combination of two varieties: (a) portal type (Pfortadertypus), and (b) the cistern type (Zysternentypus).

According to this Swiss author hematogenous dissemination should follow the laws governing general circulation, corresponding to one type or other, depending on the location of the original tumor. In the last three types he admits the existence of a filter, in the sense that the capillary network of the lung or liver can arrest the neoplastic embolus and it may thus constitute the starting point for later dissemination.

This idea was proposed at the beginning of the century by Martin B. Schmidt who in several cases of metastasis found distant neoplastic thrombi in the small arteries and capillaries of the pulmonary tissues. The thrombi described were found, from the standpoint of morbid anatomy, to represent different phases of evolution, with an initial tendency of the neoplastic cells to undergo organization and later to suffer destruction.

It is possible for these thrombi to remain for years in a latent state, and yet subsequently to give rise to late remote metastases. The liver and the lung, for purely circulatory reasons, would constitute the real filters of the neoplastic thrombi and at the same time serve as the starting point of new metastases.

Askanazi, considering the problem from

* Translated from the Spanish by Dr. James T. Case, Santa Barbara, California.

a purely defensive point of view, points out three important organs which serve as venous filters in the path of the neoplastic spread, namely, the liver, the osseous medulla, and the spleen. The existence of these organs, abundantly supplied with elements of the reticuloendothelial system, contributes in an important manner to the defense against neoplastic invasion, thanks to the highly efficient defensive and phagocytic function of the endothelium of the capillaries as well as of the reticular tissue.

Sternal Contamination. The matter of sternal contamination, the objective of our investigative work, comes up frequently for consideration in tumors of the mammary gland. The seeding can take place: (a) by way of the veins; (b) by way of the lymph stream.

(a) Direct sternal contamination (by way of the veins): The contamination in mammary carcinoma passes to the sternum by way of the local venous circulation of the mammary gland and by way of the intercostal and internal mammary vessels, or even directly. The entry of the neoplastic cells into the mammary veins takes place by corrosion of the venous walls by the tumor. This phenomenon is frequently observed in cases of malignant tumor and is due to the proteolytic action of the neoplastic cells.

From the veins of the mammary gland the accumulation of tumor cells or the neoplastic thrombus comes to rest in the intercostal veins. From this location the tumor cells have two pathways by which to spread. They may be directed anteriorly and finally empty directly into the sternum, or they may reach this bone through the internal mammary veins (see Figs. 1 and 2). If, on the other hand, the malignant cells are directed toward the posterior aspect of the thorax, they may reach the prevertebral venous plexuses and contaminate the vertebrae, the pelvis and the cranium.

Depending upon the location of the thrombus in the prevertebral venous plexus and the communications of this plexus with the vertebrae, the seeding of the spine may result in a high, medium or low vertebral colonization. This depends also on the postural tendency of the patient, the action of gravity on the thrombus, and the direction of the blood stream, as well as other physical factors of circulatory mechanical nature, which influence the thrombus at a given moment.

In the case of mammary neoplasms, direct sternal contamination by the direct venous route seems more frequent than vertebral seeding; at least, the contamination is more easily demonstrated in the sternum than in the vertebrae. The proof of the sternal seeding can be accomplished in three ways: (1) by the Gil y Gil sign; (2) by sternal roentgenography; (3) by sternal puncture. These phases of the question have been dealt with by us in previous communications.

The Gil y Gil sign is produced by pressure of the tip of the index finger against the surface of the sternum. When the sternum is altered, there is pain at the point of pressure or pain due to compression of nerve endings. Normally the sternum does not hurt when compressed. The existence of localized or diffuse pain constitutes a clue to a sternal lesion which may be brought into relief by sternal roentgenography, confirming the presence of trabecular rarefaction at the site of the painful zone. Sternal puncture in this rarefied area may show the existence of neoplastic cells.

The accompanying roentgenograms, all of them of patients with mammary carcinoma, give some idea of the lesions produced by this mode of contamination. The process is osteolytic. Extension of these osteolytic changes can be recognized.

(b) Lymphatic mode of contamination: the parasternal lymphatic intrathoracic lymphatic glands, also spoken of as the glands of the internal mammary chain, may become contaminated by way of the lymphatics connecting the mammary gland directly with the sternum. This second possibility has not yet been visualized.

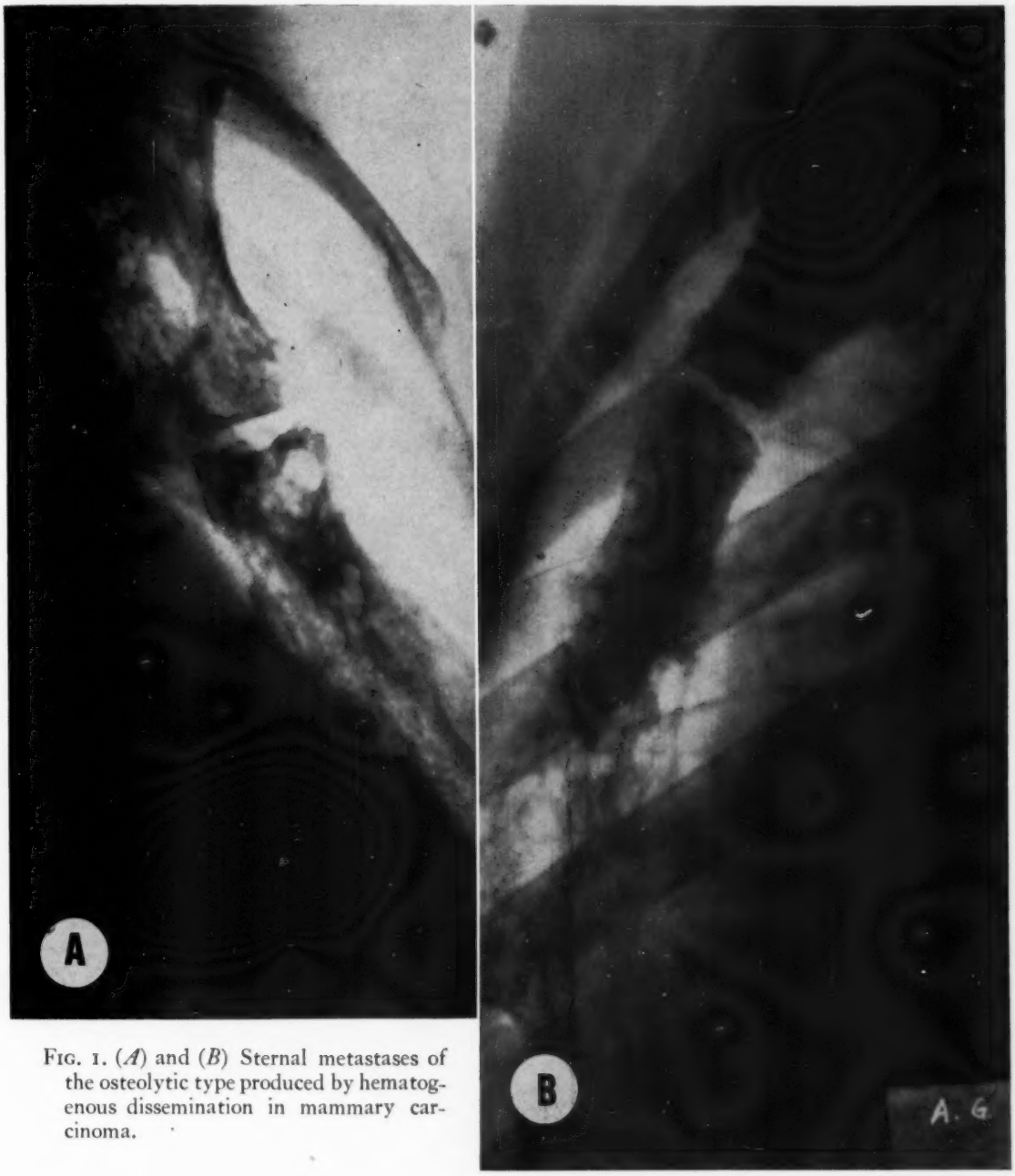

Fig. 1. (*A*) and (*B*) Sternal metastases of the osteolytic type produced by hematogenous dissemination in mammary carcinoma.

Glandular metastases in the internal mammary chain may grow to such an extent as to rupture the capsule, producing propagation of the tumor *in situ* if the involved gland is attached to the posterior aspect of the sternum. The proteolytic property of the neoplastic cells causes destruction of the periosteum of the compacta of the posterior sternal wall. This amounts to neoplastic extension "per contiguitatem." (See Fig. 3.)

This method of extension occurs in practice more often than is generally believed, although less frequently than extension by the venous pathway. Propagation of the tumor in this manner by way

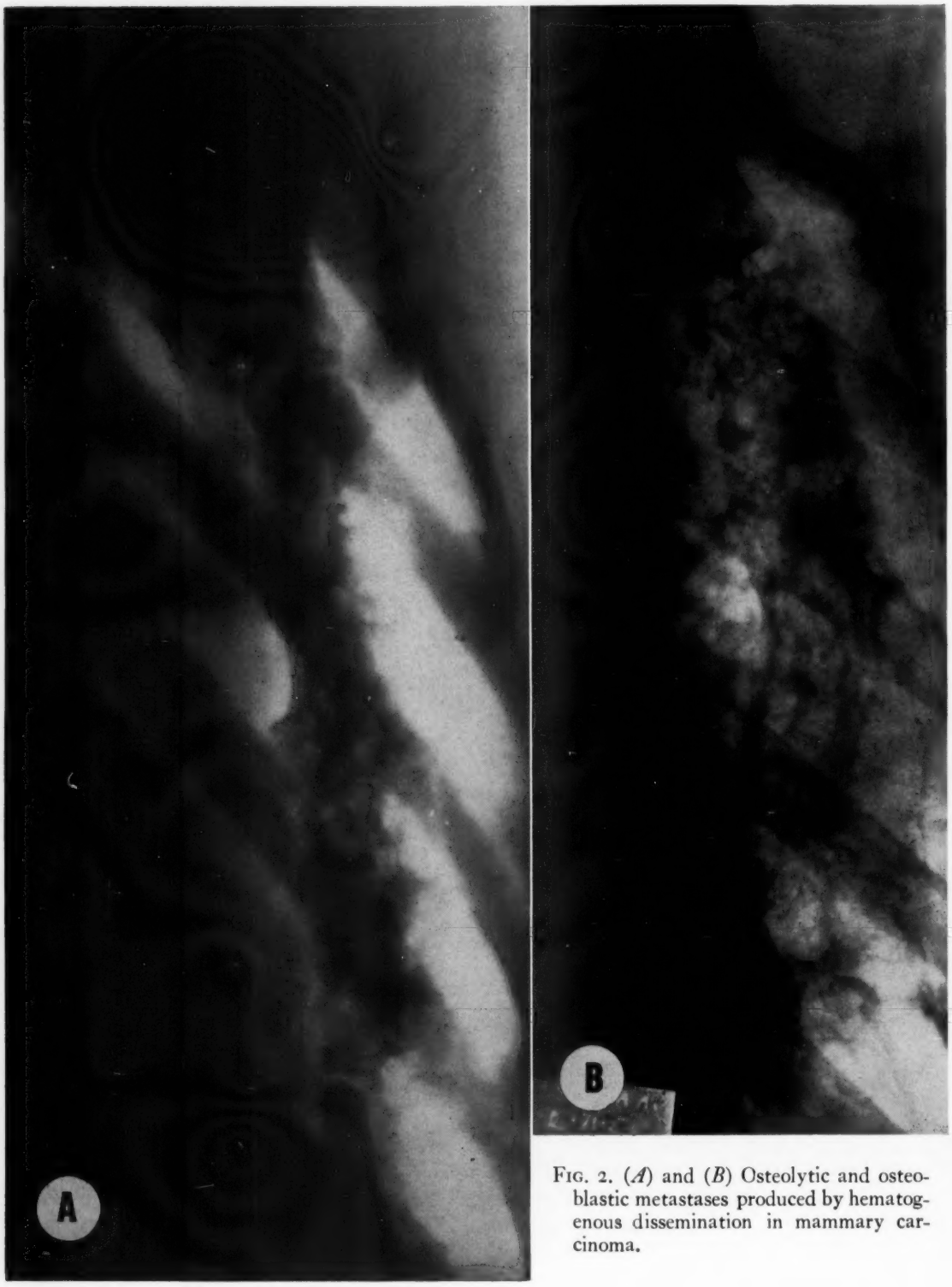

Fig. 2. (*A*) and (*B*) Osteolytic and osteoblastic metastases produced by hematogenous dissemination in mammary carcinoma.

Fig. 3. (*A*) and (*B*) Mechanism of dissemination via the lymphatics ("per contiguitatem").

of the retrosternal glands is exemplified in the accompanying illustrations.

Tumors arising in the anterior mediastinum, such as lymphosarcomas, Hodgkin's lymphogranulomas, bronchial tumors, etc., also may be spread by this mechanism.

Direct venous contamination, in spite of the fact that one is dealing with epithelial tumors, probably occurs much more often than that produced via the lymphatic route through the retrosternal glands.

In any case we have observed the existence of sternal implants in the early stages of mammary tumors (Grade 1, Steinthal). Likewise we have observed that these implants may remain dormant for many years without giving rise to symptoms (silent metastases). In either case there are very interesting prognostic and therapeutic problems to consider.

CONCLUSIONS

Sternal contamination in cases of mammary carcinoma may occur by two principal routes:

1. Directly, by the intravenous pathway, from the mammary gland to the sternum via the mammary veins and the intercostals, or from the intercostal veins to the internal mammary vein and the spongy substance of the sternum.

2. By way of the lymphatics from the breast and by the deep lymphatics of the thoracic wall to the retrosternal glands (the internal mammary glands). Rupture of the glandular capsule causes erosion of the periosteum and the compact bone of the sternum.

In the first case (extension by the venous route), the invasion of the sternal spongiosa probably precedes the destruction of the compact bone; and in the second, the sternal compacta must undergo erosion prior to the colonization of the spongiosa and, therefore, the hematopoietic tissue.

3. We think there may also be a third mode of propagation by direct lymphatic extension from the breast to the sternal spongiosa, without participation of the internal mammary glands.

4. The existence of a possible direct lymphatic pathway between the breast and the spongiosa of the sternum has not yet been observed by us, but we suspect its existence.

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ROENTGENOLOGIC SYNDROME IN THE DIAGNOSIS OF INTRATHORACIC MENINGOCELE*

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AT VARIOUS times we have had the opportunity of presenting the roentgenologic signs of intrathoracic meningocele.[3,4,5,6,7,8] In view of the fact that in this Congress there are surgeons and roentgenologists, not only from the American continents but also from other parts of the world, it seems appropriate to present once more certain considerations relating to the diagnosis of this morbid process. The success of surgical intervention, as we have pointed out in various other works already published, depends exclusively on the accuracy of the diagnosis, and this can be made only by means of the roentgenologic examination.

Noguera and Stupenengo,[17] after a most thorough study, stated that the reading of our communications enabled them, by taking as a basis the roentgenologic signs pointed out by us, to make the correct diagnosis in one case, and, therefore, they propose to unite these signs in a roentgenologic syndrome.

The existing literature indicates that the disease is none too well known, the diagnosis in the cases thus far published usually having been made at the time of the operation or postmortem.

The lack of exact diagnosis before the operation increases the difficulties of the surgeon and seriously endangers the patient, a fact to which we had drawn attention in our writings. Rupture of the pocket of the meningocele took place in all cases described, causing the death of the patient.

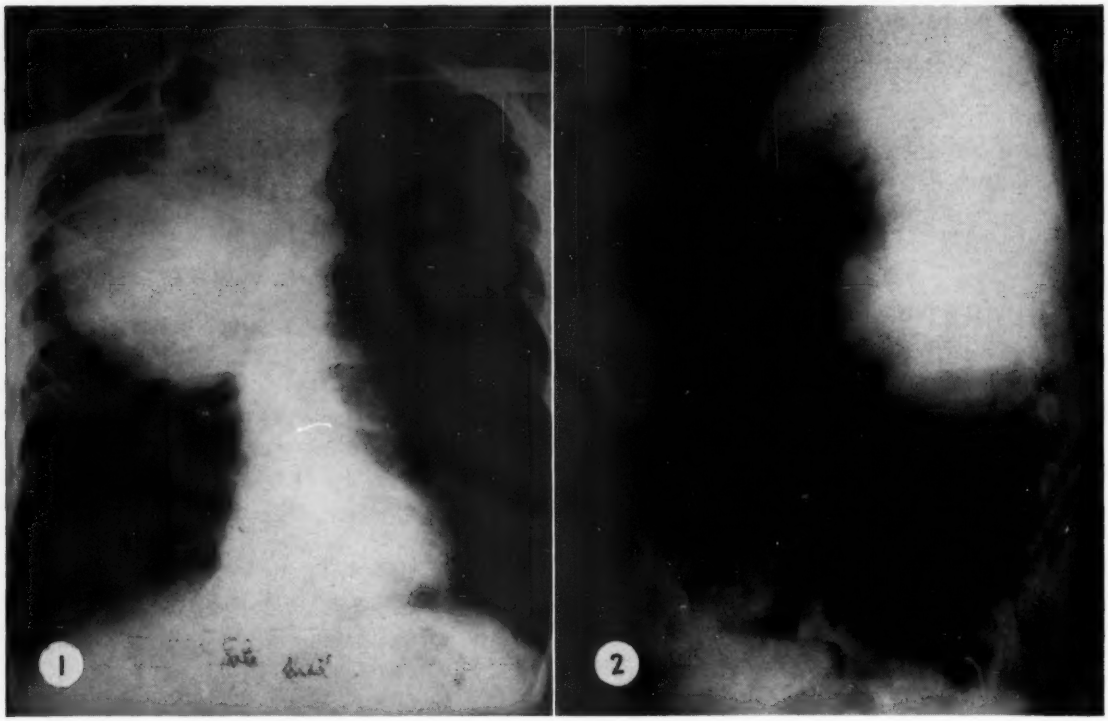
The roentgenologic diagnosis of intrathoracic meningocele is relatively simple, if one remembers the possibility of its existence and knows all the signs which comprise the roentgenologic syndrome.

Intrathoracic meningocele is manifested by the development of a tumor in the paramediastinal pulmonary field, with characteristics of benignity, regular rounded contours, with neat borders, and not bringing about any pathologic alterations in the neighboring structures. It projects medially and posteriorly as related to the vertebral column, and near it.

The tumor with the above-mentioned characteristics is always accompanied by congenital anomalies, either of the vertebrae (bifid spine), deformities of the thorax itself (ribs, sternum) or of the lungs (air cysts). Frequently it is accompanied by multiple neurofibromatosis of Recklinghausen (which raises the question of a congenital origin), which caused the majority of authors to interpret the tumor shadows as that of an intrathoracic neurofibroma. With these three signs: (1) benign tumor shadow, (2) posterior localization near the spinal column, (3) accompanied by congenital anomalies, recognized by means of ordinary roentgenograms without any other preliminary methods, the diagnosis is made without difficulty.

For the sake of illustration we present one of the cases observed by us and previously published, in which we can observe these three roentgenologic signs (Figs. 1 and 2): posterior localization of the tumor shadow near the spine; existence of congenital cysts of the lung; anomalies of the arches of the ribs and of the thoracic column (scoliosis, flattening of the vertebrae). Furthermore, the patient suffered

* Presented at the Ninth Congress of the International College of Surgeons, São Paulo, Brazil, April 26–May 2, 1954.



FIGS. 1 and 2. Roentgenograms of the thorax, anterior and lateral. Rounded shadow of regular contours, detached from the mediastinum and projecting into the right superior and posterior pulmonary field near the vertebral column. The neighboring pulmonary parenchyma does not show any alterations. On the left side, at the level of the tumor shadow, it is seen that the pulmonary radiolucency has increased and the bronchovascular arborization does not show (congenital pulmonary cyst). Dextro-concave scoliosis of the thoracic spine. Vertebral deformities.

also from Recklinghausen's neurofibromatosis.

SUMMARY

The author summarizes the roentgenologic signs that make possible the diagnosis in vivo of intrathoracic meningocele.

The three roentgenologic signs described by the author which Noguera and Stupenengo have set up as a syndrome, are:

(1) Benign intrathoracic paravertebral tumor shadow.

(2) Posterior projection near the spinal column.

(3) Associated congenital anomalies (of the lung, of the thorax, of the spine, and others).

The author points out the importance of knowing these signs in order to make safely an exact diagnosis, thus avoiding untimely surgical interventions.

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CONSIDERATIONS OF IONIZING RADIATION IN CHILDHOOD*

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A MORE appropriate title for this discussion would be "The Reflections of a Practitioner on the Use of Ionizing Radiation in Children." As a pediatrician it is far from my intention to trespass into areas of physics, biology or therapy with which this audience is so familiar and the speaker is not, but rather to present a point of view—not an original one to be sure—which I believe merits your very serious consideration. Briefly, if broadly expressed, this point of view is that the practitioner—the family physician or pediatrician—is currently in need of authoritative guidance from radiologists in order to fulfill a fundamental responsibility to his juvenile patients; namely, that the continuity of the child's growth pattern from conception to maturity must not be altered physically or psychologically as the result of disease, accident or any therapeutic measure insofar as it is within his power to prevent such an event. This responsibility must necessarily be shared, in varying degrees, by all physicians participating in the care of children.

When problems arise in the fields of pharmacology and surgery the practitioner can nearly always obtain assistance by reference to the literature and from more experienced associates. In the field of ionizing radiation in children he finds himself confused by the very meager literature available and disturbed by inflexible opinions, sometimes of a most sweeping character, regarding hazards, on the one hand, or safety on the other, among his colleagues.

A problem exists not only in the field of radiotherapy but in diagnostic roentgenology as well. The child may have his first contact with roentgen rays or radioactive isotopes prenatally by diagnostic procedures on the pregnant woman. Following birth the multiple opportunities for exposure throughout infancy, childhood and adolescence are well known. Two important facts in this regard will be recalled:

(1) The frequency of roentgenoscopy at monthly or quarterly routine health examinations is entirely at the discretion of the child's physician.

(2) There is no irradiation diary in general use as yet, not only in private practice but in hospitals, although the need for such a record has been apparent and recommended by various authors.

Results in the investigational and clinical fields pose questions that cannot be disregarded:

Investigation. To what degree may the results of studies of radiation effects in lower animals and bacteria be utilized in formulating principles to guide us for the human child?

Somatic and sex cell mutations, alterations in enzyme systems, shortening of life span, impaired fertility, carcinogenesis are among some of the well known effects produced experimentally. It is pertinent to our discussion to recall that many such studies have been performed on young animals. Thus Rugh[9] found that ovaries of young newborn mice were very sensitive to ionizing radiations from radioiodine administered to the mother and reaching the young through the milk. The ovary of the five day old mouse was more sensitive than that of the fifteen day old mouse.

Lick, Kirschbaum and Mixer[6] induced ovarian tumors in Bagg albino mice which were given whole body irradiation of 200 r at eight to ten weeks of age.

Clinical Aspect. From the clinical aspect an appraisal of serious sequelae to skin,

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crystalline lens, bone, thyroid, etc., is complicated by the fact that in most reported instances the dosage was above recognized therapeutic levels. However, there would seem to be other cases in which the individual response to average dosage was peculiarly unique

Skin: Scharnagel and Pack[10] reported the case of a boy who had been treated in a well known hospital as an infant for hyperplasia of the thymus gland and in whom multiple basal cell carcinomas had occurred in the skin of the anterior and posterior thoracic wall at five years of age.

Bone: Neuhauser *et al.*[8] studied roentgenographically the vertebrae of 34 children who had been given radiotherapy for retroperitoneal neuroblastoma and Wilms' tumors. He concluded that " . . . dosage in excess of 2,000 tissue r irrespective of the age of the child will probably produce growth disturbances." Cahan *et al.*[1] describe the occurrence of two bone cancers eight and seventeen years following radiotherapy during childhood for benign processes (osteoma and chondroma); the tumor dose in the former was 1,510 r and in the latter 1,550 r.

Lung: Garrett and Mertz[5] describe 2 cases of pulmonary metastases of Wilms' tumor treated successfully. In each case both lung fields were treated with disappearance of the lesions. The tumor dose was 1,500 r in twenty-three days and 1,600 r in twenty-two days respectively, and there was no recurrence or pulmonary fibrosis two years later.

But a child of three and a half years treated at Memorial Hospital for pulmonary metastases of Wilms' tumor developed extensive pulmonary fibrosis four months after a course of radiotherapy to both lungs, the total tumor dose of which amounted to 1,850 r.

Kidney: Zuelzer, Palmer and Newton[12] reported 3 cases of glomerulonephritis following roentgen irradiation of the renal area. The children's ages were four, three and one and a half years; the total dosages were 5,850 r, 5,200 r and 6,850 r. The children all died seven months or less from the start of the radiotherapy.

Nasopharyngeal Radium Applicator. Crowe and Loch[2] state that no deleterious effects have been observed in the use of this procedure but Schneider[11] believes that "the possibility is serious that late sequelae such as atrophic rhinitis or worse may occur."

Fowler[4] describes the occurrence of a severe epithelitis in which the question of an intramucosal carcinoma was considered. The patient had received "a course of deep x-ray therapy . . . then two years later 3 applications of the monel metal 50 mg. capsules for 8½ minutes at 3 week intervals."

Blood: The greater incidence of leukemia among radiologists and dermatologists than among their colleagues in other specialties has statistical support.[3] Lorenz,[7] in questioning that ionizing radiations could increase human incidence, makes the following statement: "Chronic irradiation produces the disease [leukemia] in mice only when *young* animals are exposed to a dosage rate to the whole body far exceeding that which the radiologists encounter in radiological work."

These observations must be compared with dramatically gratifying results obtained in the treatment of other serious cases. Some of our own experiences will be briefly referred to by me and the details of the therapy presented by Dr. Phillips.

1. A child with a primary intrathoracic neuroblastoma with metastases to the supraclavicular nodes was treated at the age of fifteen months. She was given 1,600 r (in air) anteriorly and posteriorly with regression of her tumor and remains in good health eight years from the date of therapy.

2. An unclassified sarcoma of the left leg involving the tibia and soft parts. Treated at two months of age. No evidence of disease twenty years later.

3. A spindle cell sarcoma of the thigh muscles treated at the age of two months. No evidence of disease sixteen years later.

4. An inoperable retroperitoneal neuroblastoma with early hepatic and skull metastases.

Beginning at six and a half months she was treated by combined chemotherapy and radiotherapy. She will be five years old in May, 1954, and a recent letter from her mother states her condition "most pleasing."

In conclusion, let me say that it is realized this is only a very limited discussion of a very profound subject. However, the very complexity and the ramifications implicit or suggested in the field of radiation suggest that some accepted standards of procedure be promulgated by responsible medical societies rather than individuals or institutions for guidance of the practitioner. Certain standards to govern the use of fluoroscopes in hospitals were proposed by a joint committee of several national medical societies and have been adopted by the Joint Hospital Accreditation Board.

It is not to be expected or even desired in our present state of knowledge that agreement on all aspects of the use of ionizing radiation could be realized. I am sure, however, that there are areas of acceptance, non-acceptance and partial acceptance which, if brought to the attention of the family physician, would significantly benefit present and future generations of our children.*

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* For discussion see page 626.

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RADIATION THERAPY IN PEDIATRICS*

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ALTHOUGH cancer stands third among the causes of death in children, it is nevertheless an uncommon disease, so that it often takes ten or twenty years to collect enough cases for an informative survey of each type of tumor. There were, for example, 69 cases of Wilms' tumor at the Boston Children's Hospital[5] in seventeen years, 22 cases of medulloblastoma at the Manchester Christie Hospital[11] in twenty years, and 81 cases of neuroblastoma in twenty years at Memorial Hospital,[13] New York. During such long periods methods of treatment undergo many changes, so that it is not surprising that the value of radiotherapy for cancer in children is uncertain, and its late effects on growth and function largely unknown.

The accumulated experience of radiotherapy for cancer in adults affords little guidance for its use in children, because the predominant types of cancer are quite different. In adults most of the deaths from malignant disease are due to carcinomas arising in the digestive, respiratory and genital systems; in children, about half are due to tumors, mainly of embryonic type, arising in the nervous and urinary systems,[1] and a third to leukemia.[8] Furthermore, the fortunate infrequency of childhood cancers precludes the success of an empirical approach to the evaluation of radiotherapy, whereas in adults the frequency of each of the common types of carcinoma permits the statistical comparison of different methods of treatment within a relatively few years.

CHANGING CONCEPTS OF ETIOLOGY

The behavior of carcinoma in situ, the temporary control of acute leukemia by antimetabolites, and the regression of mammary or prostatic carcinoma under hormone therapy, have rendered untenable the concept of cancer as a completely autonomous, steadily progressive new growth with an irreversible course; instead, the idea of a changing relationship between tumor and host demands increasing recognition for a better understanding of the natural history of malignant disease.

The concept of a tumor-host interaction has changed the management of cancer in childhood, because many congenital tumors (and by analogy some of those which do not become apparent until varying times after birth) seem to be due to aberrations in the processes which control normal embryological development and subsequent growth. The importance of the tumor-host relationship is suggested by many observations: the continued growth of a few hemangiomas, in contrast to the spontaneous disappearance of the majority; the spontaneous regression of established malignant tumors[14] (*e.g.*, hepatic metastases of neuroblastoma,[16] pulmonary metastases of Ewing's tumor[10]); the more or less late appearance of cancer in teratomas and other initially benign tumors, and conversely the occasional change of malignant neuroblastoma into benign ganglioneuroma[2]; the spread of the age incidence of typical childhood cancers into adult life (*e.g.*, Wilms' tumor, neuroblastoma, medulloblastoma, acute leukemia), and conversely the occurrence of a cancer normally confined to adults in a child (*e.g.*, a malignant melanoma in a four year old boy with an adrenal cortical carcinoma); the better prognosis of some types of cancer in infants than in older children (*e.g.*, Wilms' tumor[5]); the very late recurrence of an apparently cured tumor (*e.g.*, medulloblastoma recurrent seventeen years after treatment[12]); the inability to predict the response to treatment of tumors of the same pathological type (*e.g.*, the lack

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Fig. 1. Patient of Dr. George T. Pack. Congenital spindle cell sarcoma of leg; roentgen therapy when two months old, tumor dose 3,600 r in 25 days. (*A*) Roentgenogram before treatment. (*B*) Roentgenogram at age sixteen. Normal development of bones except for 1 inch of shortening.

of correlation between radiation dose and tumor response, and unexpected regression after very little treatment[14] or after treatment had apparently failed[13]).

The weight of such observations has changed the management of children with malignant disease, because so long as a fatal outcome can be postponed, there may be hope of a natural mechanism of tumor control developing or increasing. Thus the total care of the child becomes as important as the treatment of localized tumors, with particular attention being given to nutrition in the widest sense and to the use of systemic agents which may favorably affect the tumor-host relationship.

CHANGING CONCEPTS OF RADIOSENSITIVITY

Radiotherapeutic thought and practice have been greatly influenced by two general formulations: (a) that radiosensitivity is directly proportional to rate of growth and inversely proportional to degree of differentiation, and (b) that the radiosensitivity of malignant neoplasms is proportional to that of the analogous normal cells. There are, however, so many exceptions to these "rules" that their clinical application should not be too dogmatic, particularly in pediatric practice, where predictions of radiosensitivity or radioresistance based on pathological criteria should not unduly influence clinical judgment. For example, in Desjardins'[3] classification of normal tissues in order of radiosensitivity lymphocytes are the most radiosensitive and nerve cells the most radioresistant, yet the corresponding malignant tumors, lymphosarcoma and neuroblastoma, are about equally radiosensitive. Or to take another kind of exception, a keloid is usually far more radiosensitive than a spindle cell sarcoma, and a hemangioma than a hemangiosarcoma. Yet another aspect of this question is the gen-

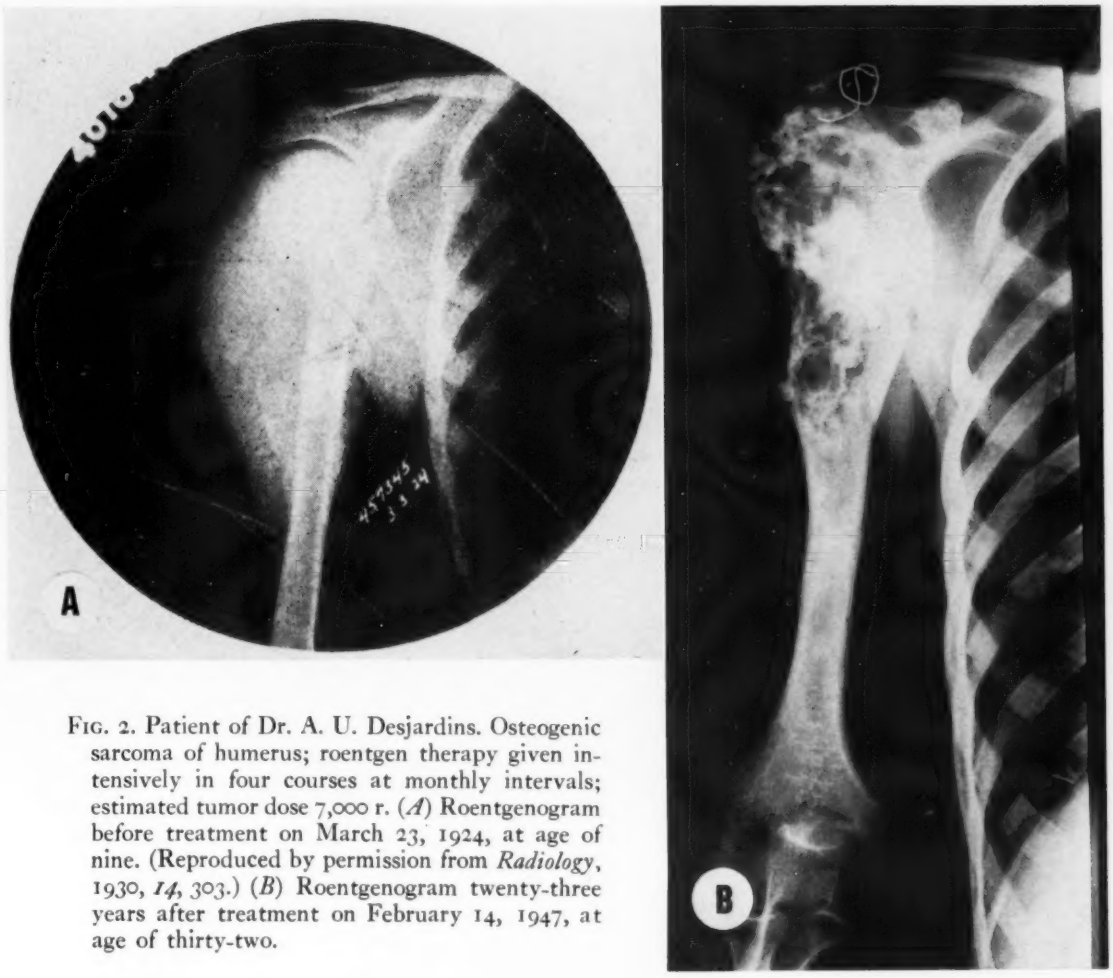

FIG. 2. Patient of Dr. A. U. Desjardins. Osteogenic sarcoma of humerus; roentgen therapy given intensively in four courses at monthly intervals; estimated tumor dose 7,000 r. (*A*) Roentgenogram before treatment on March 23, 1924, at age of nine. (Reproduced by permission from *Radiology*, 1930, *14*, 303.) (*B*) Roentgenogram twenty-three years after treatment on February 14, 1947, at age of thirty-two.

eral assumption that normal tissues[7] and malignant tumors[9] are more radiosensitive in children than in adults, and that radiation dosage should therefore be scaled down the younger the patient. With the possible exception of babies in the first few months of life, I have not found that the effects of a given dose of radiation vary with age; epilation of the scalp (1,000 r), brisk skin erythema (3,000 r), mucositis and radiation diarrhea (2,500 r), and pneumonitis (2,000 r) all occur equally in children and adults at approximately the same dose levels and time intervals. Neither have I found that the effective tumor dose for those types of cancer which occur in both children and adults, and which show sufficient temporary response for observations to be made (such as Ewing's tumor, embryonal carcinoma of the testis, medulloblastoma, rhabdomyosarcoma), varies in any way with age.

It is possible that children's tissues might be relatively more radiosensitive than those of adults, but the difference is offset by a greater power and faster rate of recovery in children. However, in embryological development it has been found that radiosensitivity is not a simple function of age, but that each developing organ passes through a critical period of peak sensitivity.[6] Thus it is possible that in postnatal life also the radiosensitivity of different tissues is too complicated a phenomenon to show a linear relationship with age. For example, the irradiation of a spindle cell

Legend on opposite page.

sarcoma of the leg in a two month old baby did not greatly interfere with subsequent growth (Fig. 1), but after irradiation of the humerus for osteogenic sarcoma in a nine year old girl its subsequent growth was completely arrested (Fig. 2).

The study of late radiation effects introduces another aspect of radiosensitivity, for the absence of any immediate reaction after irradiation does not preclude later manifestations of radiation damage. A big difference between pediatric and adult practice is the much longer life expectancy of successfully treated children, during which unexpected late sequelae of irradiation may occur. In the treatment of cancer such risks must be taken, but they can hardly be justified in nonmalignant conditions. For example, Duffy and Fitzgerald[4] noted that 9 of 28 children with thyroid cancer had received roentgen therapy for an enlarged thymus in infancy. The association may be only coincidental, for in Warren's[15] 200 cases of thyroid cancer in patients under twenty years of age only 1 was noted as having had previous irradiation of the thymus. There are of course some instances where radiotherapy is necessary in benign conditions (Fig. 3), but it is surely only prudent to limit the necessity as much as possible.

Fig. 3. Congenital hemangioma. (*A*) Appearance at age of one year on July 9, 1951, three months before roentgen therapy. (*B*) Appearance on March 25, 1952, five months after roentgen therapy, 1,550 r in 19 days. (*C*) Appearance at age of three and a half on January 8, 1954.

It is clear that much more extended observations are required before the place of radiotherapy in pediatrics can be determined, not only as to its actual value in the treatment of childhood cancers, but even more as to its late effects on growth and development. Although to this audience I thought it might be more useful to emphasize the uncertainties, I do not think that there is any doubt that the outlook for cancer in children is less grim than it was twenty years ago, and that radiotherapy has contributed to this improvement.

SUMMARY

1. Malignant disease in children, although uncommon, ranks third among the causes of death.

2. The importance of the tumor-host relationship in childhood cancers is illustrated by numerous examples.

3. The radiosensitivity of normal and malignant tissues is not directly related to the age of the patient.

4. No evidence was found that the effective tumor dose varies according to the age of the patient.

5. Although the value of radiotherapy is uncertain, it has an essential part in the present management of childhood cancers, together with supportive measures, surgery and chemotherapy.

6. The late effects of radiotherapy on growth and development are at present largely unknown.

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DISCUSSION OF PAPERS BY DR. HAROLD W. DARGEON AND DR. RALPH F. PHILLIPS

Dr. Vincent P. Collins, Houston, Texas. These have been fascinating papers, and it is a privilege to discuss them. But if Dr. Phillips had difficulty in finding other material in the literature, who is to offer pertinent discussion to the two men who have had most experience in treating tumors of childhood?

One of Dr. Dargeon's main concerns is protection and Dr. Taylor's earlier paper contains these views: First, any radiation exposure can be minimized, and it should be. Second, radiation exposure must be viewed sensibly so as not to impair the efficiency of the method or jeopardize the result.

This morning we heard that 2 per cent operative mortality associated with exploratory thoracotomy was acceptable. The incidence of induced malignancy in patients successfully treated for tumors is very much lower. In the treatment of cancer by any method, we will accept some incidence of complication as the necessary price for even limited success. The accidents of treatment or diagnosis that happen —the unfortunate, untoward result of treating benign lesions—can be corrected by education and open criticism.

The risk that troubles us most lies in the radiation exposure of diagnostic procedures or the use of radioisotopes. That meaning it may have for us in the future is conjecture. It has been very well stated that the practice of medicine is the balancing of competing risks in treatment of disease to achieve an improvement in the patient's outlook or survival. In the case of the individual patient or the broad problem, the physician will give more weight to the immediate and evident benefit than the distant and uncertain risk.

As long as fluoroscopy is believed to add information to physical examination it will continue to be used, and restriction is impractical. Since most radiologic equipment is owned by practitioners other than radiologists, interference on the part of radiologists in this field is apt to be looked upon as in the interest of something other than the patient's protection.

Both Dr. Dargeon and Dr. Phillips have stressed the unusual or exceptional examples of long duration, spontaneous regression, or unusual effects of treatment. These instances should be examined for significance. Survival curves show a slender extension of the curve far to the right, indicating that there is a predictable probability that cases of long duration will occur. This applies even to untreated tumors, and the effect of treatment in prolonging the curve to the right is difficult to weigh.

I wonder if some of you have been disturbed, as I have been, to find or observe that the remarkable results of cure and survival are not necessarily limited to the most experienced hands. Sometimes the result seems unrelated to the effort put into the treatment. Still, if we cannot ascribe the results purely to diligence and experience, these two factors have a broad field for development and application in the prevention of complications.

Dr. Phillips mentioned that a somewhat better prognosis is found in the younger age group. Relatively few tumors are observed at the time of birth but this is one circumstance where we can be sure of the maximum possible duration of the tumor. The tumor that is present at birth cannot have a duration of more than nine months. To develop a tumor in that length of time really means a tremendously rapid rate of growth. It has been my impression that, if recurrence is to develop, those tumors which come to clinical attention earliest are also those in which there is the most rapid recurrence and the earliest time to death. I wonder if Dr. Phillips has had similar experience.

Dr. Phillips and Dr. Dargeon have had a unique opportunity to see so many patients in this group. I think it would be very appropriate if the Society could consider Dr. Phillips' suggestion to pool experience with childhood tumors. Only thus may the benefit of the broad experience be extended to the few patients one individual may see.

PRIMARY CARCINOMA OF THE URETER

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PRIMARY carcinoma of the ureter has always been considered a very rare disease but the recent reports in the literature suggest that it should be changed from the rare to the infrequent class. The disease has apparently received very little attention in the radiologic literature since the author has been able to discover only one reference in the radiologic journals.[3] All other references were discovered in urological, surgical, or cancer journals, or in non-specialized publications. It might therefore be of advantage to radiologists to become better acquainted with primary carcinoma of the ureter.

Historically, the first case was reported in France by Rayer in 1841. The first English language report was by Davy in 1884. At the turn of the century only 8 cases had been found and they were all discovered at autopsy. Albarran, in 1902, made the first preoperative diagnosis. In 1934, 61 cases had been reported in the literature and Scott, in 1934, had discovered 180 cases and added 2 of his own. In 1948 the total was brought up to 196 cases. In a thorough review of the literature Senger and Furey,[5] in 1953, arrived at a total of 310 cases, including the 2 cases they presented. A search of the literature for cases not reported by these authors revealed reports in 1951, 1952, and 1953. Bowen and Atherton[1] present 2 cases, Campbell[2] has 1 case, Soloway[6] discovered 7 cases at the Chicago Cook County Hospital, Keen[4] found 6 cases, and Wiggins-Davies and Elwood[7] add 3 cases. When the 3 cases presented by the present author are added we arrive at a grand total of 333 cases. Thus it can be seen that during the past five years 137 new cases have been reported; admittedly this is no longer a rare disease and it may well be on the increase as all malignancies appear to be. If a more careful search for these unusual tumors were made it is entirely possible that the number of cases would be even higher.

Primary tumors of the ureter have been found 3 times in 13,854 autopsies at the Vienna Pathological Institute and twice in 22,000 urologic admissions at the Johns Hopkins Hospital. Soloway[6] found 4 cases in 26,410 autopsies at the Chicago Cook County Hospital since 1930.

Pathologically, primary cancer of the ureter is a carcinoma of the transitional type of epithelium found in other parts of the urinary tract such as the renal pelvis and the urinary bladder. The ureteral tumors can possess all the features of tumors in the renal pelvis and the urinary bladder. According to Senger and Furey[5] 86.5 per cent of the tumors of the the urinary epithelium occur in the bladder while 8.4 per cent occur in the renal pelvis and ureter. Seventy-five per cent of the neoplasms of the ureter are carcinoma while 21 per cent are benign papilloma and the remaining 4 per cent are made up of sarcoma, hemangioma and fibroma. Roughly one-half of the carcinomas are papillary while the other half show a solid type of growth. The neoplasms have a tendency to be multicentric in location and may be found widely separated in the urinary tract, but most often only one localization is found. If situated low in the ureter the tumor may grow downward and protrude into the bladder at the ureteral orifice so that it can be seen and biopsied cystoscopically. The tumor may be a solid pedunculated growth occluding the ureteral lumen, a sessile papillary carcinoma with invasion of the ureteral wall or a diffuse papillary growth. The papillary growths can encircle the ureter to spread early, extensively, and quickly. The rate of growth frequently depends upon the degree of differentiation of the tumor. According to Soloway[6]

metastases were found in 62 per cent of reported cases; in order of frequency, these metastases occurred in regional and distant lymph nodes, the liver, the lungs, the bones, the kidneys, the adrenals, the spleen, the brain, the pancreas, and the skin.

The tumor bleeds freely and causes varying degrees of ureteral obstruction. Dilatation of the ureter above the tumor, and hydronephrosis are frequent complications. Some of the more invasive tumors have been known to produce perforation of the ureter.[3]

The tumors are found predominantly in the lower third of the right ureter in from 50 to 67 per cent of cases depending on the reporting author. The reason for this favorite location has given rise to numerous fanciful theories but none have ever been substantiated, and they need not be discussed in this report. In 19 cases since Senger and Furey's[5] report where the location of the tumor was described, there were 8 cases in the lower third of the right ureter. In the present report two tumors were found in the left ureter, and one on the right side.

Clinically a symptomatic triad has been described consisting of hematuria, pain, and a palpable abdominal mass. The most frequent symptom is that of bleeding which is often intermittent, ceases for no apparent reason, only to recur, and is often painless, especially at the onset of the disease. The pain may be due either to the obstruction of the ureter with back pressure symptoms upon the upper urinary tract, or to direct invasion of the ureter. The abdominal mass is the distended hydronephrotic kidney. In Senger and Furey's article hematuria was found in 92 per cent of 130 cases, pain in over 50 per cent of cases, and a palpable mass in only 20 per cent of cases.

Cancer of the ureter was found in patients twenty-two to eighty-nine years of age (Soloway). The greatest number is seen in the sixth and seventh decades and in 65 per cent of cases the male sex was afflicted.

The treatment of choice consists of a complete nephro-ureterectomy, preferably with removal of a cuff of bladder at the ureterovesical junction. The average survival time is 21.1 months. Preoperative and postoperative radiation therapy appear to be of no value.

The diagnosis of primary carcinoma of the ureter may be suspected from the clinical history. The typical case may be pictured as in a man, sixty years of age, with intermittent hematuria, pain in the flank of a continuous nature and a palpable mass in the renal area. The ultimate diagnosis, however, can be made much more probable by roentgenologic studies.

A survey film of the abdomen will show typically a moderate enlargement of the kidney on the affected side without any calculi in kidney or ureter. The intravenous urogram will reveal a lack of renal function or delayed function on the involved side. It must be remembered, however, that if some increasing opacity of the enlarged kidney occurs during the half hour following injection of the contrast medium it is often very advantageous to obtain delayed films in one hour, two hours, four, six, eight, or even twenty-four hours. These films may well delineate the hydronephrosis and hydroureter down to the level of the tumor. If success is obtained in delineating the ureter one should search for irregularity in the outline of the column of contrast medium where it impinges against the neoplasm. The carefully done retrograde pyelogram is usually the most informative study. Very often the ureteral catheter is arrested at the level of the tumor and induces considerable bleeding. Ureterograms will then outline the lower edge of the tumor showing either an irregular shadow, a sharp cut-off in the column of contrast medium or an abrupt stricture with shaggy irregular margins.

If the catheter can be passed above the tumor an irregular filling defect of varying length will be seen. The defect may have overhanging edges above or below similar to the appearance produced by an annular

carcinoma of the colon. One of the cases in this report was correctly diagnosed because of this appearance. The solid pedunculated growths are most apt to completely occlude the ureter so that the catheter cannot be passed beyond the tumor, while the papillary growth will produce a shaggy irregular filling defect in the ureteral lumen with only a partial obstruction. When extensive invasion of the ureteral wall has occurred the catheter may perforate the ureter and the ureterogram will reveal extravasation of the contrast medium into the periureteral connective tissue. This occurred in one of the cases reported by Holmes.[3] If multiple defects are discovered in the ureter and in the renal pelvis the diagnosis becomes almost certain. It may be difficult to obtain a good detailed ureterogram especially when the tumor is situated in the lowermost portion of the ureter. At times the ureter can be filled satisfactorily with contrast medium by placing the patient in the Trendelenburg position; however, it may be necessary to use a special ureteral catheter which occludes the lower ureter and prevents escape of the medium introduced into the upper ureter.

The differential diagnosis to be considered is that of nonopaque calculi, blood clots, benign ureteral stricture, ureteritis cystica and ureteral tuberculosis.

The nonopaque stone can be very confusing on a single examination. It will usually obstruct the ureter to prevent passage of the catheter beyond it. In repeated pyelograms the stone will usually have moved to a different location. The author recently had a case in a fifty year old man with continuous left flank pain for six months and a palpable left kidney. The excretory urogram showed obstruction of the upper third of the ureter with an irregular border at the obstruction but there was no visible stone. On retrograde pyelography a catheter was easily passed up to the renal pelvis and excellent ureterograms showed an irregular filling defect about 3 cm. in length in the upper third of the ureter with dilatation of the kidney and ureter above the lesion. Thick inspissated urine was withdrawn from the catheter and sent to the laboratory for cellular study. The microscopic study revealed clumps of cells very suspicious of neoplasm. At surgery, however, no tumor was found and the ureter showed a calculus with thick muddy amorphous material above the stone.

Blood clots usually do not obstruct the ureter on intravenous or retrograde urograms. They may remain in the same location in the ureter on repeated studies and their length and irregular configuration may prove very confusing.

Benign strictures may also resemble carcinoma very closely but they do not produce severe hematuria and the ureter above the stricture is usually markedly dilated.

Ureteritis cystica does not obstruct the ureter or produce filling defects of the magnitude observed with carcinoma. It usually involves a long segment of the ureter, and, as a rule, it also involves the urinary bladder where it is seen by the cystoscopist.

Ureteral tuberculosis ordinarily occurs with well evident tuberculosis in one or both kidneys and need not cause much difficulty in differential diagnosis.

In regard to calculi, it must of course be realized that urinary calculi and ureteral carcinoma can coexist and do not exclude each other. The tumor, of course can be readily diagnosed by the cystoscopist if it protrudes from the mouth of the ureter into the bladder where it is accessible for biopsy. Of all the diagnostic methods this direct biopsy constitutes the only completely reliable method. One may obtain valuable help from a cellular study of the urine aspirated from the ureteral catheter but cellular studies are very difficult to interpret and may lead to erroneous conclusions. The pyelographic studies as seen above are very suggestive of a diagnosis of carcinoma of the ureter but only rarely can they be considered as completely conclusive.

I wish to present 3 cases of primary carcinoma of the ureter. The first is a case of Dr. H. A. Jarre's of Grace Hospital, Detroit, Michigan. The second case was seen by Dr. A. K. Payne of the Foote Memorial in Jackson, Michigan, Dr. Jarre's first resident in radiology. The last case was seen by the author who was Dr. Jarre's second resident. Only Dr. Jarre's case was conclusively diagnosed roentgenologically before surgery.

REPORT OF CASES

Case 1. This case was contributed by Dr. H. A. Jarre of the Department of Radiology, Grace Hospital, in Detroit, Michigan.

A white female patient had had no significant history until 1941 when, at the age of thirty-three, she suffered a fracture of the left hip in an automobile accident. Following this trauma she consistently complained of pain in the left kidney area. Because of the persistent pain she consulted a physician who referred her to a gynecologist. Finally, the continued distress led the gynecologist to perform an exploratory laparotomy in 1942. No disease could be discovered in a thorough exploration of the abdominal organs except for a marked retroversion of the uterus which was therefore suspended. No relief from the pain followed this surgery and the patient continued until 1944 when she had an acute sore throat. She did not consult a physician at this time but tried self-medication with sulfanilamide tablets for ten days. The sore throat subsided but she then experienced a dull ache in the left side of the abdomen of sufficient severity to prevent sleep. This led her to consult a physician who told her she had pyelitis and administered some pills which gave little or no relief. There was also some frequency and urgency of urination which disappeared after one week; no bleeding on urination occurred.

She was admitted to the Grace Hospital in November, 1944, now aged thirty-six. The temperature on admission was 104° F., and the patient appeared acutely ill. The physical examination revealed no significant findings. The impression on admission was that she had some impacted sulfanilamide crystals in the left urinary tract.

Intravenous urograms revealed a normal right urinary tract and a failure of function on the left side. Retrograde pyelograms showed a rather long stricture at the junction of the middle and lower thirds of the left ureter with dilatation of the ureter above the stricture and hydronephrosis of the left kidney (Fig. 1). The transition from relatively normal to pathological ureter was quite abrupt, showing an overhanging shelf at the upper margin of the defect. The appearance was analogous to the change produced in the colon by an annular carcinoma and Dr. Jarre made a diagnosis of carcinoma of the ureter.

Fig. 1. The stricture-like lesion in the left ureter is well shown. The lesion has practically the same features of annular carcinoma such as would appear in a carcinoma of the colon.

The patient was operated on four days later through a left kidney incision. The kidney was found to be rather large and was removed, leaving the ureter intact. The ureter was then freed down to a level shortly below the pelvic brim where some adherent fibrous tissue was encountered causing considerable difficulty in freeing the ureter. Nevertheless the ureter was freed to a point shortly below the adhesions

Fig. 2. Almost complete obstruction of the upper right ureter with only a thin comma-shaped streak of contrast medium in the ureter. Partial filling of a hydronephrotic kidney.

where it was doubly ligated, phenolized, and excised.

The surgical specimens showed a kidney with hydronephrosis and multiple parenchymal abscesses. The ureter showed, at the lower end of the specimen, a thick wall containing tumor tissue. On microscopic study this proved to be a highly undifferentiated primary carcinoma of the ureter.

Twelve days following the surgery the patient was again operated on through a left anterior abdominal approach and the remainder of the ureter was resected. No additional tumor tissue was found.

The patient's pain at last was gone and she felt so well after recovery from the surgery that she married, against the advice of her physician. She remained well until 1947, when she began to suffer from backache and "gas on the stomach." The pain continued for two months and she was re-admitted to Grace Hospital with a palpable mass in the left flank. There were no visible neoplastic metastases on roentgen examination of the chest and abdomen. Surgery was performed in April, 1947, revealing an extensive left retroperitoneal mass extending from the duodenum down to the brim of the pelvis. The mass was densely adherent and was found to surround the major vessels and to displace the descending colon. It could not be removed and a small piece was excised for biopsy. The microscopic study again revealed a highly undifferentiated carcinoma.

The patient died at the age of forty in January, 1948, seven years after she first experienced left abdominal pain and thirty-eight months following removal of the neoplasm.

Case II. This case was generously contributed by Dr. A. K. Payne of the Department of Radiology of the Foote Memorial Hospital, in Jackson, Michigan.

The patient, a man aged fifty-eight, was seen in 1948 because of intermittent hematuria of two months' duration accompanied by pain in the right flank. There were also occasional bouts of fever. No other relevant factors were elicited from the history and physical examination.

Retrograde pyelograms showed a normal left urinary tract and a hydronephrosis on the right. The right renal and ureteral lumina were not well filled (Fig. 2). There was, however, a definite impression of narrowing and tortuosity of the upper right ureter of unknown etiology. The possibility of some type of neoplasm was suspected and surgery was performed. The kidney and upper portion of the ureter were removed.

The pathological specimen revealed a pyohydronephrosis, and a tumor which occluded the upper inch of the ureter almost completely. Histopathologically the ureteral tumor proved to be a moderately well differentiated primary papillary carcinoma of the ureter.

The patient at the time of this writing remains alive and well, five years after removal of the cancer.

Case III. A fifty-eight year old man was admitted to the Holy Cross Hospital, Detroit, Michigan, in April, 1952, with a complaint of severe intermittent painless hematuria for the past three weeks. He also had a positive serological test for syphilis and a moderate degree of arterial hypertension. There were no other significant findings in the history or physical examination. No masses could be felt in the abdomen and a roentgenogram of the chest showed nothing unusual.

A retrograde pyelogram revealed an obstruction on the left side to both the ureteral catheter and the contrast medium at the level of the last lumbar vertebra. The ureter widened for about 2 cm. below the lesion and the contrast medium was interrupted in a straight line across the lumen of the ureter. No cause for this abrupt occlusion of the ureter was seen on the film (Fig. 3).

Intravenous urograms were obtained two days later showing a marked delay in excretion of contrast medium from the left kidney. A film obtained two hours following the intravenous injection of the medium revealed a moderate degree of hydronephrosis on the left side with a faintly visible outline of a tortuous mildly dilated ureter down to the level of the fourth lumbar disk (Fig. 4).

Thus, the obstruction was outlined from above and below. The etiology was thought to be the result of either a nonopaque calculus, an old inflammatory process in the ureter, or a neoplasm of the ureter.

At surgery the left kidney was somewhat enlarged and adherent. In freeing the kidney a tumor of the adrenal about 4 cm. in diameter

Fig. 3. Abrupt obstruction of the left ureter at the level of the fifth lumbar vertebra. The obstruction produces a straight line across the ureter.

Fig. 4. Two hour film in intravenous urography. A very faint delineation of a mildly distended left ureter ending at the level of the fourth lumbar disk can be seen.

was found and was removed along with the kidney. The ureter was freed down to the level of the fifth lumbar vertebra where a pyriform type of tumor was found involving the entire wall of the ureter. A frozen section of a portion of the tumor revealed a malignant lesion. The ureter was ligated below the pelvic brim and was removed down to this point. Another incision was then made in the lower left abdomen and the remainder of the ureter was removed extraperitoneally.

The pathologist's examination of the specimens showed hydropyonephrosis, a benign adenoma of the adrenal, and a primary papillary transitional cell carcinoma of the ureter of Grade 3 differentiation.

There were no postoperative complications and the patient underwent a course of deep radiation therapy directed to the left abdomen.

The patient returned to the hospital in June, 1953, because of a palpable mass in the left flank. A chest roentgenogram demonstrated no disease but a film of the abdomen showed obliteration of the left psoas muscle shadow. A surgical exploration of the left retroperitoneal

tissues showed extensive adhesions but revealed no visible recurrence of the cancer. Several pieces of tissue were removed for biopsy and again no neoplasm could be found. When last heard from, nineteen months after removal of the cancer, the patient was alive and apparently well.*

CONCLUSIONS

1. Primary carcinoma of the ureter is not a rare but is an infrequent disease with a total of 333 cases now appearing in the world literature.

2. The carcinoma is a solid or papillary growth which tends to obstruct chiefly the lower third of the right ureter and metastasizes widely.

3. The clinical findings are chiefly hematuria, pain, and a palpable enlarged kidney.

4. The retrograde pyelogram is especially valuable in diagnosing the lesion which can produce a complete obstruction or an irregular filling defect in the ureteral lumen. Intravenous urograms are of less diagnostic value.

5. Reports of three new cases are presented.

* In April, 1955, three years after the discovery of the ureteral cancer, this patient died of injuries sustained in an automobile accident and an autopsy revealed no evidence of malignancy.

Holy Cross Hospital
Detroit 34, Michigan

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PRELIMINARY EXPERIENCES WITH A 50 GRAM CONVERGING BEAM RADIUM UNIT*

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WITHOUT going into either the earlier history of radiation therapy or probable therapeutic value of the radiation produced at extremely high voltages, it would seem a fair premise to state that gamma rays, so far, represent the most effective proven quality of radiation in the treatment of malignant tumors. (In our free use of the term "gamma" in this article we mean specifically the gamma radiation from radium as used ordinarily in telecurietherapy, or comparable radiations from other radioactive substances, or roentgen rays in the higher voltage levels.) The practical gamma emitters for clinical therapy, at present, are radium element; radioactive cobalt 60; and supervoltage roentgen rays produced at something over 2 mev. Each source undoubtedly has some practical advantages peculiar to itself.

After two and a half years of work we would like to present some initial observations based on our experiences in the operation of a 50 gram converging beam radium unit.

Before proceeding to a description of the engineering features of our unit, we hasten to point out that we are not competitors with the other gamma-equivalent sources mentioned, on a patient-volume basis. We believe, however, that we have certain peculiar advantages that permit of our handling a limited volume of clinical material accurately and efficiently. Our source of energy is constant and the mechanism for operation is mechanically simple.

We are interested in doing a better job than has been possible heretofore in some of the more malignant, more radiation resistant, or surgically unfavorable types of cancer. We aim at contributing something toward a greater ultimate curability in these types of growth—and with less of shock and deforming disability. Beyond that we are anxious to improve the long-term palliation in some of the incurable cases and to render more effective the short-term palliation.

In short, we hope, with the unique equipment at our disposal, to be able to set certain patterns of therapy which can be duplicated on a "wholesale" basis by other gamma or allied sources of radiation which may be available in greater volume or quantity.

The Radium Beam Unit was designed by, and constructed under the immediate supervision of, Gioacchino Failla, Sc.D., Director of the Radiological Research Laboratory, Columbia University. It contains the 50 grams of radium in the form of radium sulfate divided into twenty-five 2 gram capsules which are distributed equally spaced, in a stainless steel ring 30 cm. in diameter. The radium capsules themselves are of monel, with an outer jacket of steel to protect against mercury. When the radium is in a treating position, each capsule coincides with a conical collimating channel through the lead shielding at the bottom of the Beam Head. The capsules and collimating channels are angled inwardly approximately 23 degrees from the vertical, so that the twenty-five individual beams come together at a focus 35 cm. perpendicularly below the plane of the radium ring, the distance from a single capsule to the focus being 38.1 cm.

There are several advantages to this arrangement. If the radium were to be used

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FIG. 1. Radium sulfate salt is contained in monel tube with an outer steel jacket.

as a single source, either the source would be very thick, with a small cross section, in order to simulate a point source, or the radium would have to be spread out over a comparatively large area. With a thick source, a large part of the radiation would be absorbed by the high filtration of the intervening radium itself. With a large flat source, the sizeable penumbra would be objectionable. With twenty-five individual sources, collimation of the radiation is accomplished more easily, and, since the separate beams do not overlap completely until they reach a distance of 35 cm. below the plane of the radium, the radiation dose to any point on the skin is much less than that at the focus. The 35 cm. distance between sources and focus was determined assuming a 25 cm. source-skin distance to be reasonable for an "ideal" tumor depth of 10 cm. The diameter of the combined beams at this depth is about 7 cm. A longer source-focus distance would reduce the output at the tumor, while giving a greater relative depth dose. A shorter distance would reduce the amount of space between lead and skin or reduce the lead for protection and collimation.

In the treating position, the radium-carrying ring is at the bottom of a steel cylinder surrounded by lead. A 1/16 inch steel plate forms the bottom of the steel cylinder and the radiation enters the collimating channels through this. In order to cut off radiation when setting up patients, etc., the ring is raised through a pool of mercury approximately 14 cm. deep which then acts as a shutter beneath the radium. Additional protection is afforded by the lead at the bottom of the container, since the capsules are not in direct alignment with their individual channels except when in a treating position. The amount of radiation escaping directly beneath the Beam Head is then less than 6 mr/hr. The motion of the radium-carrying ring is controlled from outside the room, with an interlocking electric switch on the door such that entering the room automatically causes the radium to rise into its protected or "safe" position. The walls of the Beam Head are of lead and steel approximately 21 cm. thick, affording this protection between the nearest radium capsule and any point outside the container, while mercury and additional lead are between more distant capsules.

The movement of the radium-carrying ring is controlled by a rack and pinion driven by a motor through a worm gear. Rollers guide the motion, and a heavy spring is compressed by the motor after the ring reaches the bottom, thus forcing out any mercury which might remain between a capsule and the steel and absorb some of the radiation. The radium is raised by reversing the motor. Limit switches automatically stop the motor at the "on" or "off" positions after the respective spring has been compressed by a predetermined amount. There is also a manual control wheel by which the ring could be raised in the event of a power failure. To insure that each capsule is accurately centered over its corresponding channel, the ring as it comes down fits over a tapered pin in the center which keeps it centrally adjusted. Also, the ring is prevented from turning by a rod parallel to its axis and line of motion. The entire assembly for raising and lowering the ring can be removed in case of needed

repairs without any necessity for disturbing the radium.

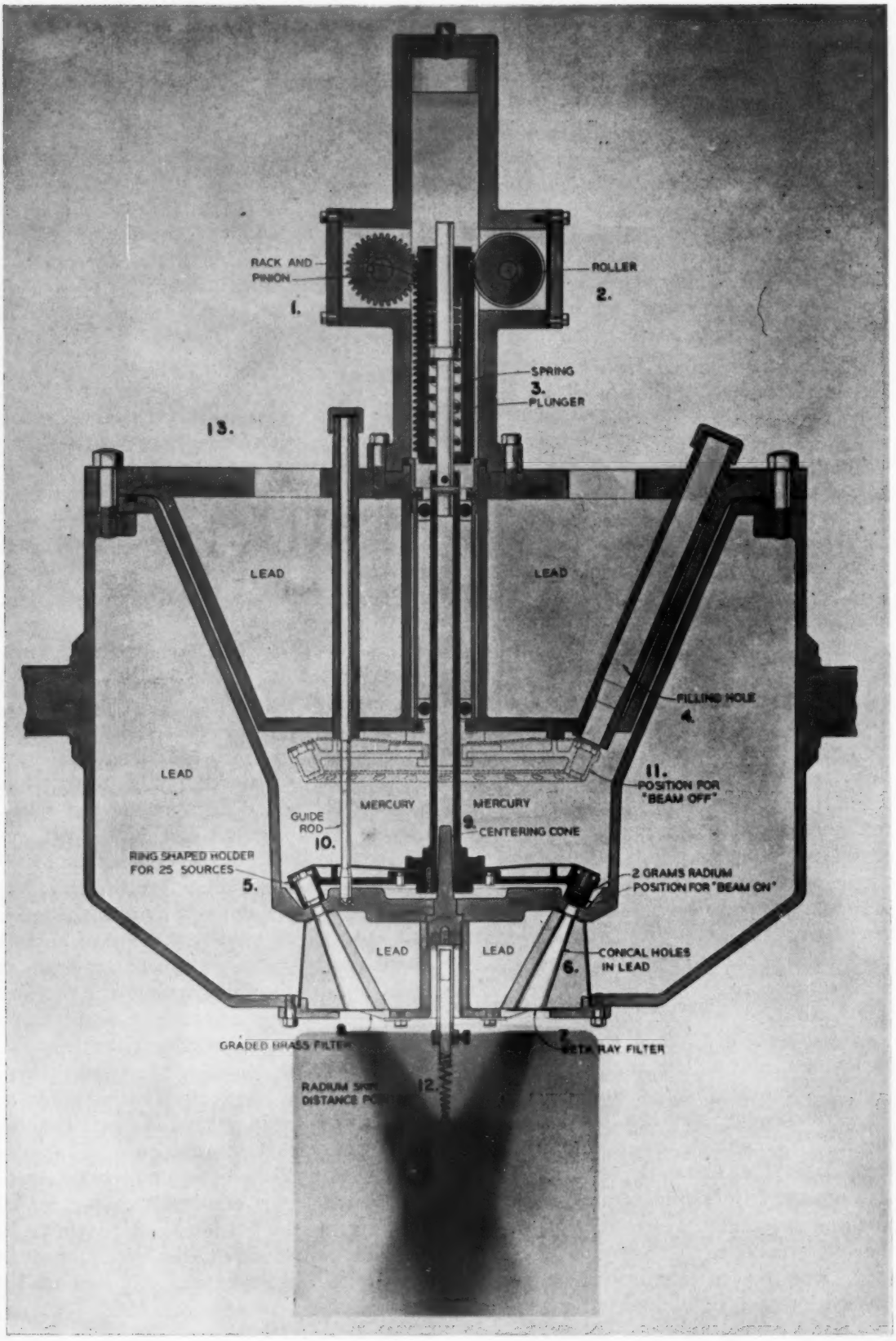
In order to place the radium capsules in the ring, the top portion of the unit was sent to Belgium attached to a rough lead bottom shield. There, each capsule was individually inserted into position through the filling hole in the top of the container, the ring then being rotated to the position of the next capsule. Meanwhile, the permanent bottom of the Beam Head was installed in the beam room here, suspended from rollers on a ceiling track, and filled with mercury. Then it was necessary only to hoist the top and radium-carrying portions of the Beam Head out of the shipping container by means of rigger's equipment brought down through a trap door in the ceiling of the treatment room, move the permanent bottom of the Beam Head under the top part by controls from outside the room, and lower the top.

The beam room itself has walls of concrete 2 feet thick and is entered through a ½-inch-lead-lined door and a maze. An observation window consists of a truncated cone of water 2 feet thick through which patients can be seen from outside during their treatments. The Beam Head is mercury tight and can be rotated completely around; however, it is generally used at any angle between its vertical and horizontal positions only, since this provides all the angulation necessary. Although the container can be moved across the room, in practice it has been left in one place in good view of the observation window and the hydraulic treatment table moved. The treatment table can be raised or lowered electrically and also tilted, thus facilitating patient setting up. The angle of tilt of the table is determined by a level and protractor arrangement attached to the side of the table. This angle, as well as the angle of the Beam Head from the vertical and the distance from the bottom of the Beam Head to the skin of the patient necessary to put the focal plane at the tumor level (measured along the center pointer), can be prescribed for each individual patient and reproduced at each successive treatment.

The twenty-five sources cannot give more radiation at the focus than would a single source, and this output is reduced by some self-absorption of the salt, and the absorptions of the monel and steel in the capsule, the steel plate holding the mercury, a brass beta-ray filter on the outside of the bottom of the Beam Head, and the amount of tissue intervening between the Beam Head and the focus, which amount depends on the particular set-up for a patient. When the focus is 10 cm. below the skin, the output is 3 roentgens per minute. There is, however, a central higher point of radiation, about 7.5 cm. above the focus, where the inner edges of the twenty-five beams begin to cross, since the distance from sources to this point is less than that from sources to focus. Thus, the isodose curves obtained with the radium unit are very different from those obtained with other sources of radiation, being somewhat similar to those recently encountered in horizontal, or "short axis," rotation therapy. The effect of the high point has been considerably lessened by a graded brass filter which fits on the bottom of the Beam Head and extends half way out over the brass beta-ray filter covering the twenty-five beam apertures, thus reducing the radiation in the inner half of the ring without appreciably lowering the dose at the focus.

The experience with this peripheral filter suggests the possibility of using the same principle at irregular positions or sectors of the periphery of the combined beam in order to more accurately meet the peculiar needs of various anatomic irregularities.

It will at once be apparent that the size and shape of the circular beam with which we are working lends itself more advantageously to certain groups of cases than to others. It is well adapted to many of the mouth and upper mucous membrane tract growths and it is admirably suited for irradiation of the bladder and prostate. In the same way it is excellent for certain of the limited but anatomically-located inoperable lung carcinomas.


RACK AND PINION
1.
ROLLER
2.
SPRING
3.
PLUNGER
13.
LEAD
LEAD
FILLING HOLE
4.
LEAD
MERCURY
MERCURY
11.
POSITION FOR "BEAM OFF"
GUIDE ROD
10.
9.
CENTERING CONE
RING SHAPED HOLDER FOR 25 SOURCES
5.
2 GRAMS RADIUM
POSITION FOR "BEAM ON"
LEAD
LEAD
CONICAL HOLES IN LEAD
6.
GRADED BRASS FILTER
BETA RAY FILTER
7.
RADIUM SKIN
DISTANCE POSITION
12.

Multiple beams can be coordinated for uniform irradiation of long oval areas such as the entire mediastinum in lung or esophageal carcinoma. In similar fashion the female pelvis may be uniformly irradiated, with or without including the uterine cervix, depending on whether or not local radium has been used to care for the cervix.

For very limited areas, such as, especially, the intrinsic larynx alone, our beam is in our judgment larger than necessary.

These differences in size and shape of anatomic fields suggest the desirability of different shapes of converging beam fields to meet more advantageously the probable tumor distribution problems in different groups of the major types of cancer.

In other words, it is our opinion that a large gamma source would be more efficient divided between several sizes and shapes of converging beam patterns rather than placed in one single large unit.

With our unusual multiple beam arrangement the skin reactions are rarely a matter of concern. In lung cancer for instance, the exit dose gives nearly as much reaction as on the side of entrance but only after a level of 6,000 to 8,000 gamma roentgens tumor dose has been reached.

In lung cancer, damage to normal lung tissue—radiation pneumonitis and fibrosis—does not occur at anywhere near the level of that with conventional high voltage roentgen radiation. In terms of tissue dose it would seem to be about the ratio of 2:1 or even 3:1 in favor of the gamma radiation put in by this method.

FIG. 3. Beam Head without covering top, showing motor-driven mechanism for lowering radium through mercury from safe position to treating position and for angulating Beam Head.

One of our most spectacular lung cases which we hope to carry on a long-term palliative basis had an advanced Pancoast type tumor of the right apex with almost complete destruction of the first rib and a fixed metastatic node mass in the supraclavicular space. A radium beam dose slightly over 10,000 gamma r in fifty-nine days has controlled the primary lesion; and radium element needle transfixion has controlled the neck mass to the extent of

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FIG. 2. Engineer's drawing of cross section of Beam Head: *1*, rack and pinion for controlling motion of radium-carrying ring up and down; *2*, guiding roller; *3*, spring compressed to force out mercury at bottom of pool when radium is in treating position; *4*, filling hole through which radium was inserted in Belgium; *5*, treating position of radium-carrying ring, showing position and angulation of radium capsule; *6*, conical collimating channel through lead; *7*, brass beta-ray filter covering bottom of Beam Head; *8*, removable graded brass filter to reduce central high point of radiation; *9*, cone for centering radium-carrying ring; *10*, guide rod to prevent rotation of ring; *11*, "off" or "safe" position of ring at top of mercury pool; *12*, central pointer along which radium-skin distance is measured; *13*, location of machinery on top of Beam Head, concealed by cover.

Lead, encased in stainless steel, surrounds the unit, and the assembly of the Beam Head by bolts in the upper corners of the diagrammed Beam Head can be seen. As actually viewed in the treatment room, the cylinder is extended upward by a cover which conceals the gearing and motor placed on the top of the Beam Head (*13*) so that only the very top of the plunger housing shows.

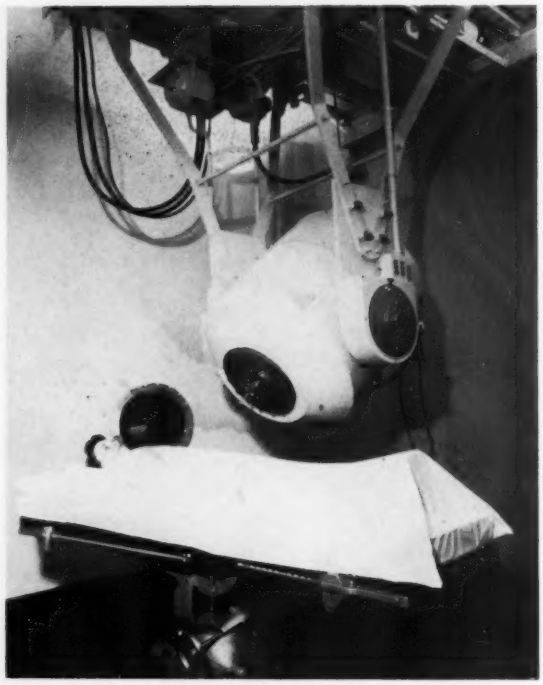

Fig. 4. Radium Beam Unit is supported on I-beam track under ceiling. Unit is mechanized and can be moved across room on track. Beam Head is angled and patient in place on table ready for final positioning.

relief of pain and restoration of limited arm function. The most interesting feature is that after this total dose there is complete restoration of the right first rib.

We have reason to anticipate less bone damage by this quality of radiation and to this end we have treated two adamantine tumors of the lower jaw, hoping to control them entirely by this means. We do not, however, know the limits of tolerance as between flat bones and long bones, or adults vs. children and adolescents. A girl of twelve years with a fibrosarcoma of the upper end of humerus, recurrent and inoperable except by interscapular thoracic amputation, made an excellent start on slightly over 7,000 gamma r tumor dose in forty-five days. After a month, 1,150 gamma r was added, followed by cessation of repair and some bone reabsorption, but with beginning repair well under way again at the end of four months.

On the other side, an adult over forty years with an epidermoid carcinoma, Grade 2 of the sphenoid and with very extensive

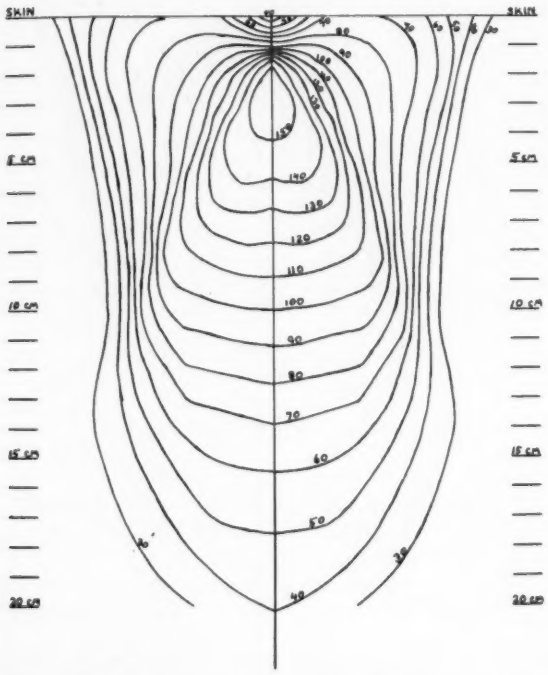

Fig. 5. Isodose curve without filter. Focus is 10 cm. deep below surface of skin. Dose is in percentage of dose to focus; high point is about 150 per cent.

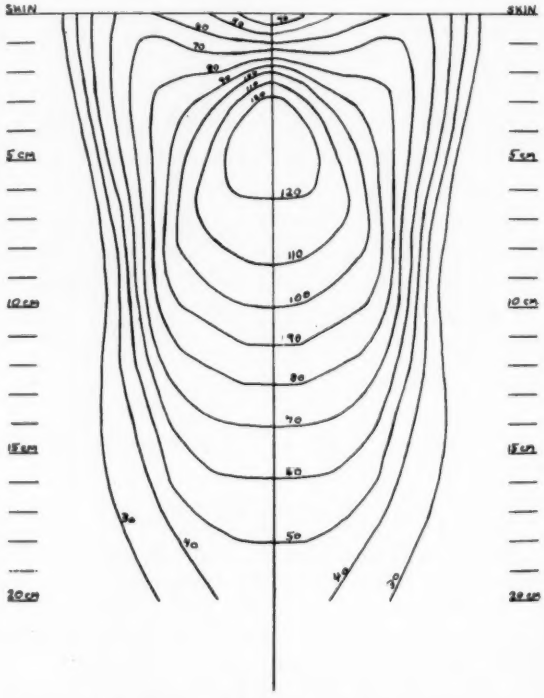

Fig. 6. Isodose curve with filter. Focus is 10 cm. deep below surface of skin. Dose is in percentage of dose to focus; high point is about 120 per cent.

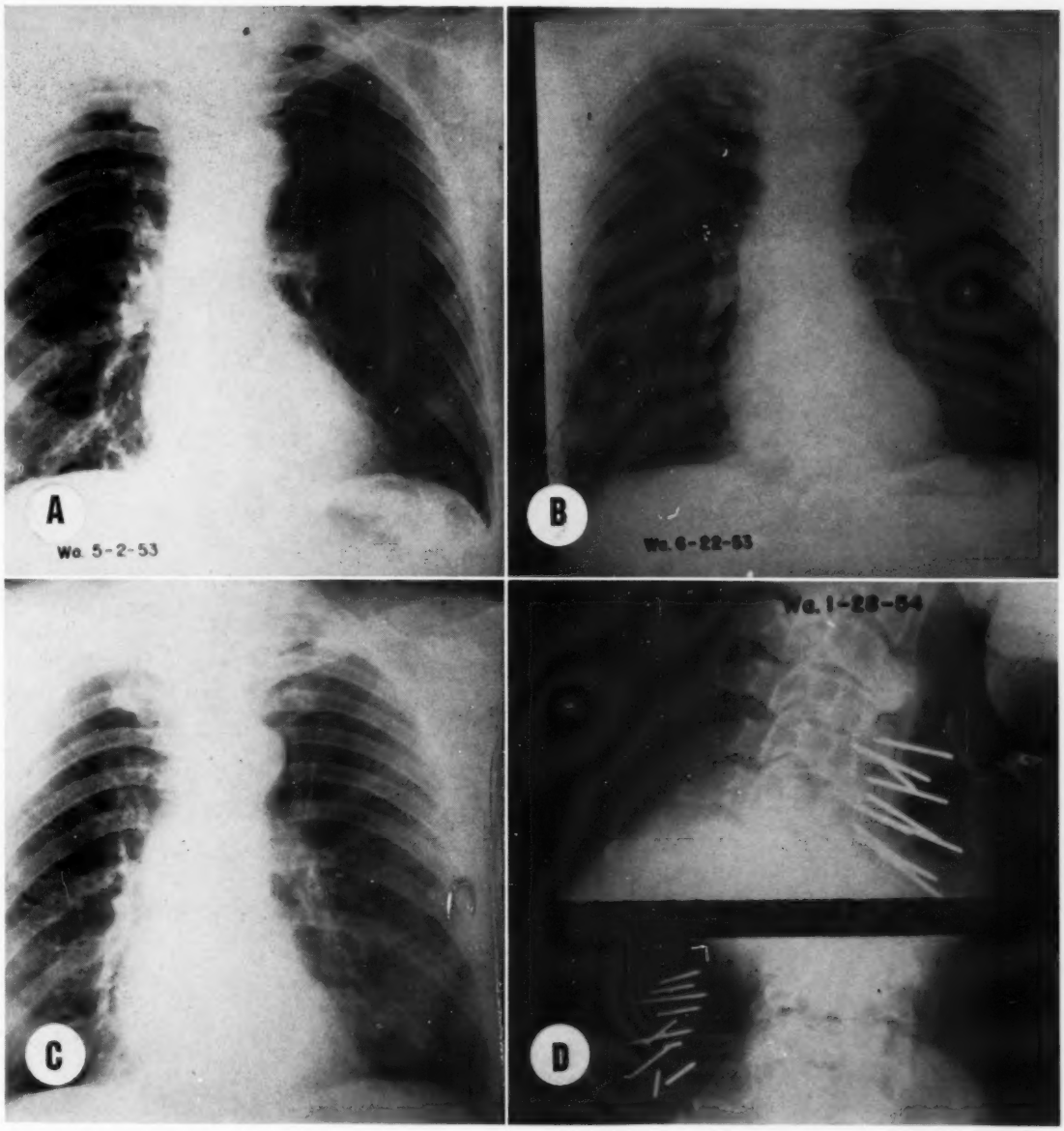

FIG. 7. Patient with advanced Pancoast type carcinoma of right apex of lung and with supraclavicular lymph node. (*A*) shows mass in the apex and extending into neck, with destruction of the first rib, at beginning of treatment. (*B*) was taken six weeks later, and shows little change. (*C*) Roentgenogram taken six months later, demonstrating the regeneration of the first rib. The final two films (*D*) and (*E*) show anteroposterior and lateral views of the radium needle implant in the neck mass.

bone destruction in the floor of the middle fossa of the skull, has not only complete growth control, but almost complete bone repair as well, after two years; and after 2,400 r tumor dose—high voltage roentgen rays at 200 kv., 80 cm. distance, and 2 mm. copper equivalent filter—plus 5,400 gamma r six weeks later, and over a four week period. A large percentage of these cases in the nasopharynx and sphenoid die, not from failure of good high voltage roentgen radiation to control growth, but from low grade chronic and subacute osteomyelitis in bone that has been damaged beyond repair by the conventional type of high voltage radiation.

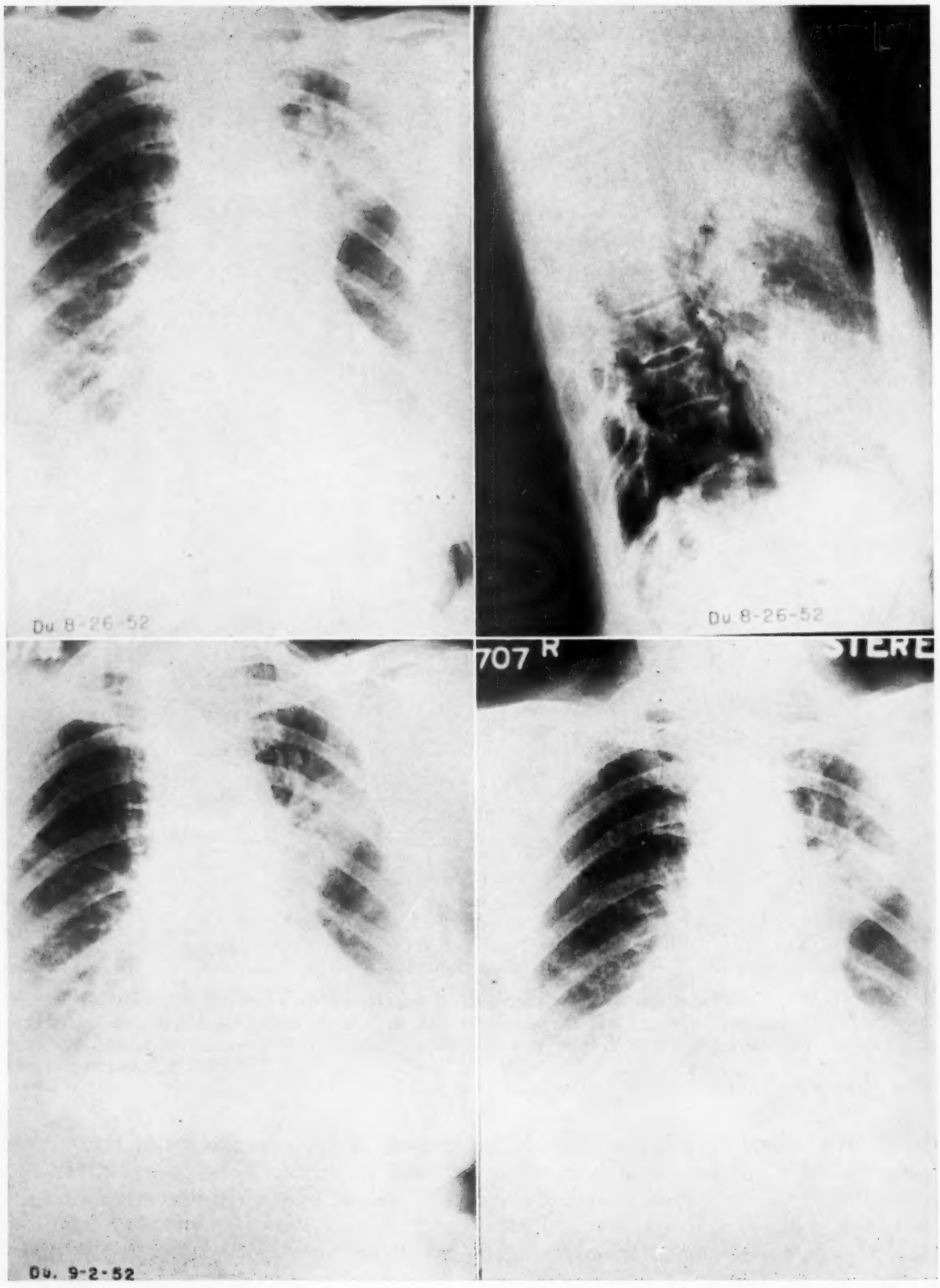

FIG. 8. A woman, aged sixty-eight, with cancer of the lung in left upper lobe, main bronchus, and hilus, who received 7,500 r in 22 days, September, 1952. The upper two films show the atelectasis present at start of treatment, the lower two films show little change six weeks later.

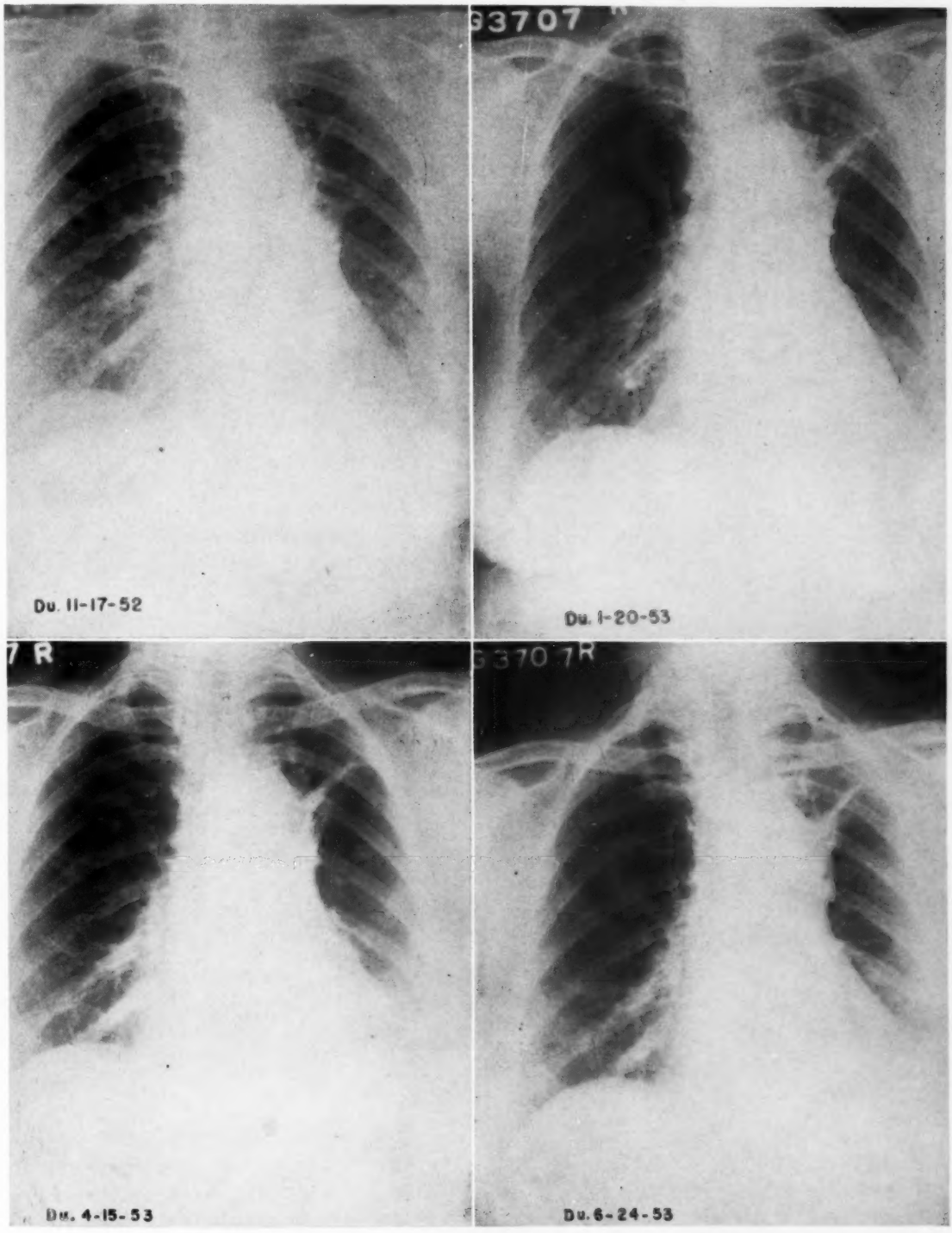

Fig. 9. Four roentgenograms of the same patient as in Figure 8 taken over the following eight months showing the gradual movement of the interlobar fissure superiorly and into the mediastinum.

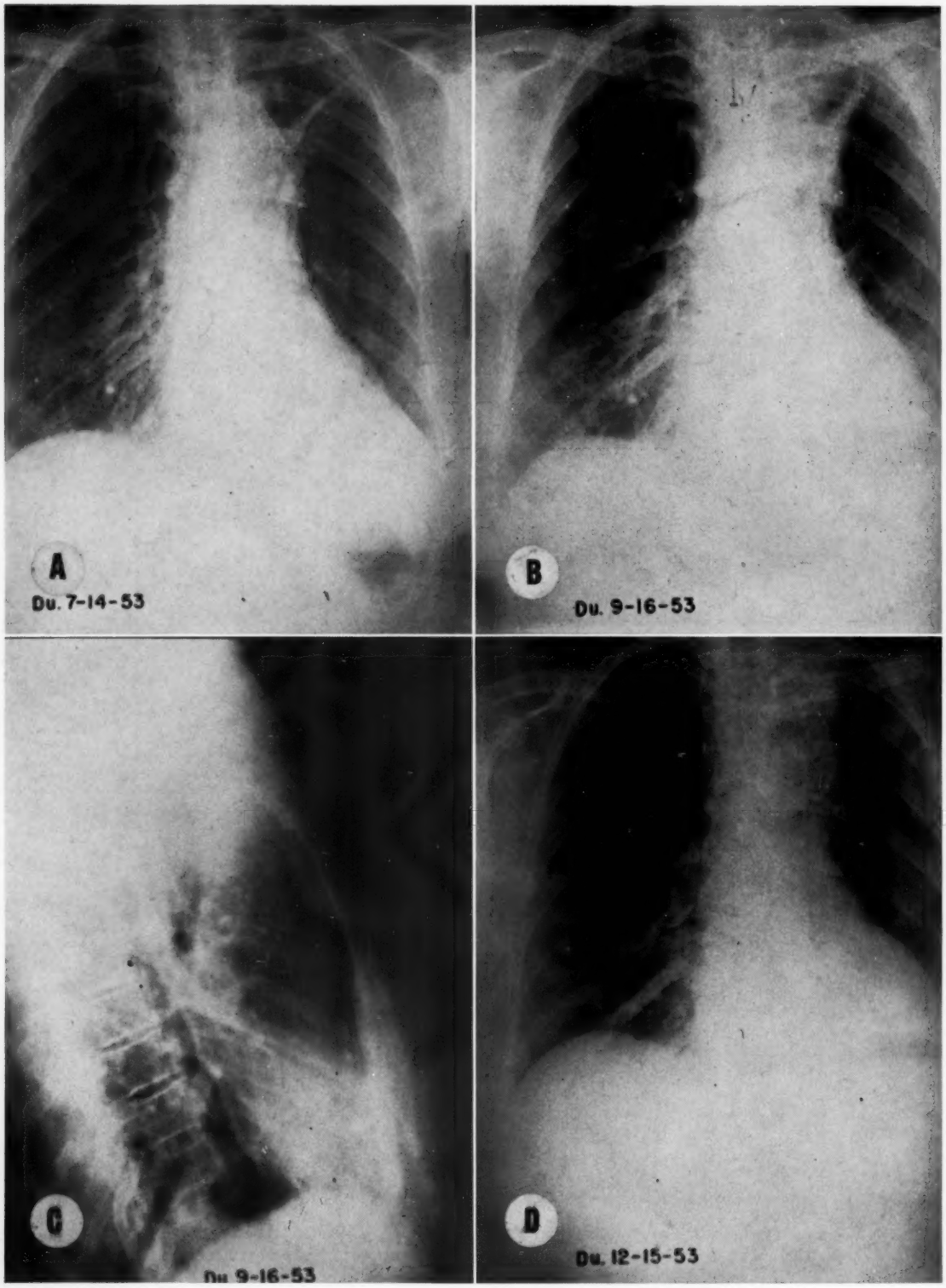

FIG. 10. Follow-up films of the same patient as in Figures 8 and 9 taken (*A*) July, 1953; (*B*) and (*C*) September, 1953, and (*D*) December, 1953. The fissure is out of sight, the left apex contracted without any gross fibrosis in the upper lobe.

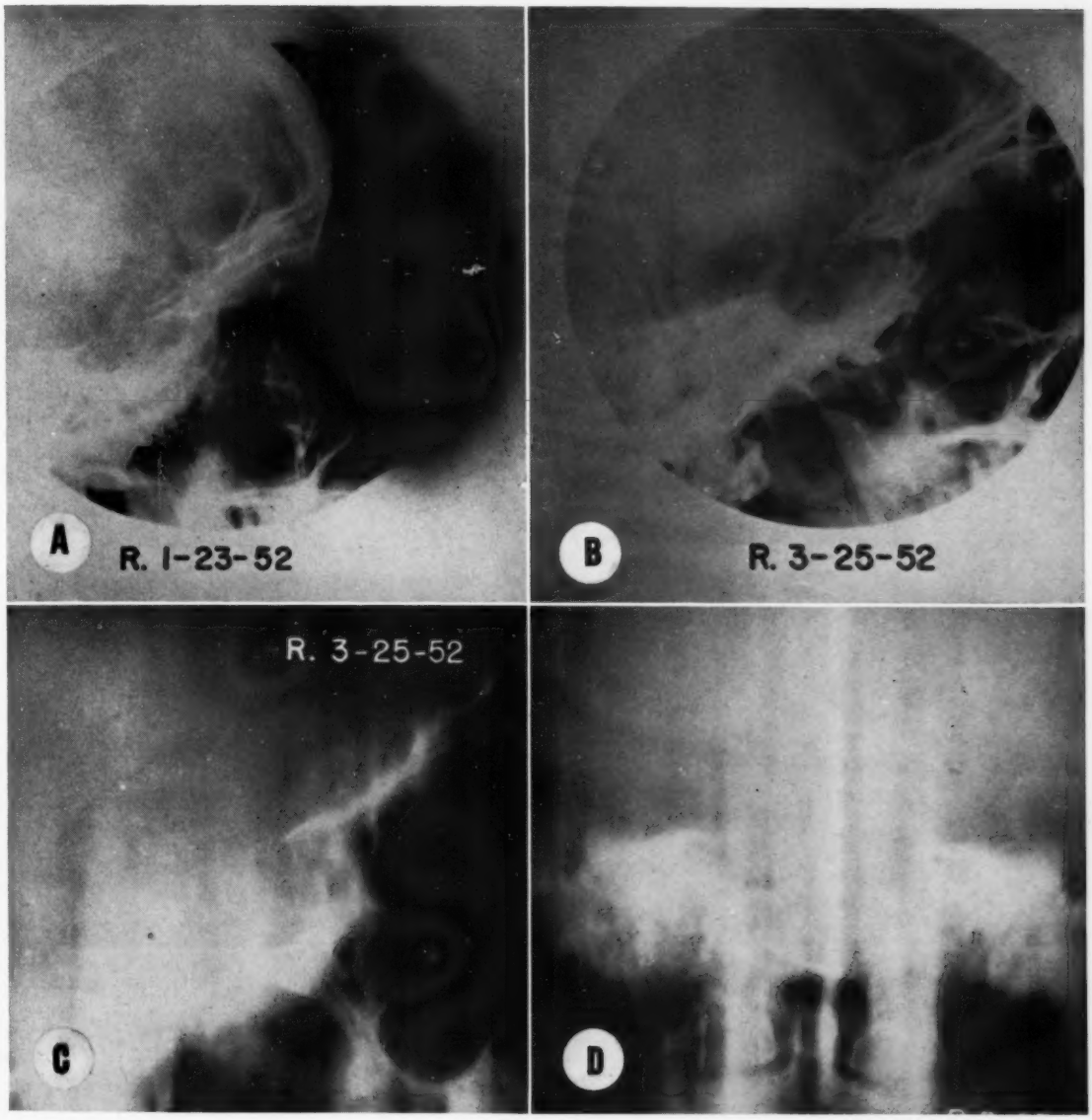

Fig. 11. A male, aged forty, with Grade 2 epidermoid carcinoma of the sphenoid sinus with extensive bone destruction in the floor of the middle fossa of the skull. (*A*) and (*B*) show the initial destruction in the zone of the pituitary fossa and the sella turcica. (*C*) and (*D*) are lateral and anteroposterior laminagrams taken at the same time.

Our limited experience with esophageal carcinoma suggests that at least a measure of growth control with maintenance of continuity of the lumen can be effected. The dosage must be high but the rate of delivery is, we believe, open to question. At present it is our impression that the esophageal carcinoma patient—elderly, weak, anemic and moderately toxic—gets on better with prolonged, but lesser quantity per week, radiation than in most other malignant groups.

Indeed we are becoming more convinced that the entire question of total optimum treatment interval may require restudy and revision. This impression has come about through our attempts to effect complete control of very extensive epidermoid carcinoma in the mouth, pharynx and hypopharynx by Radium Beam Therapy alone.

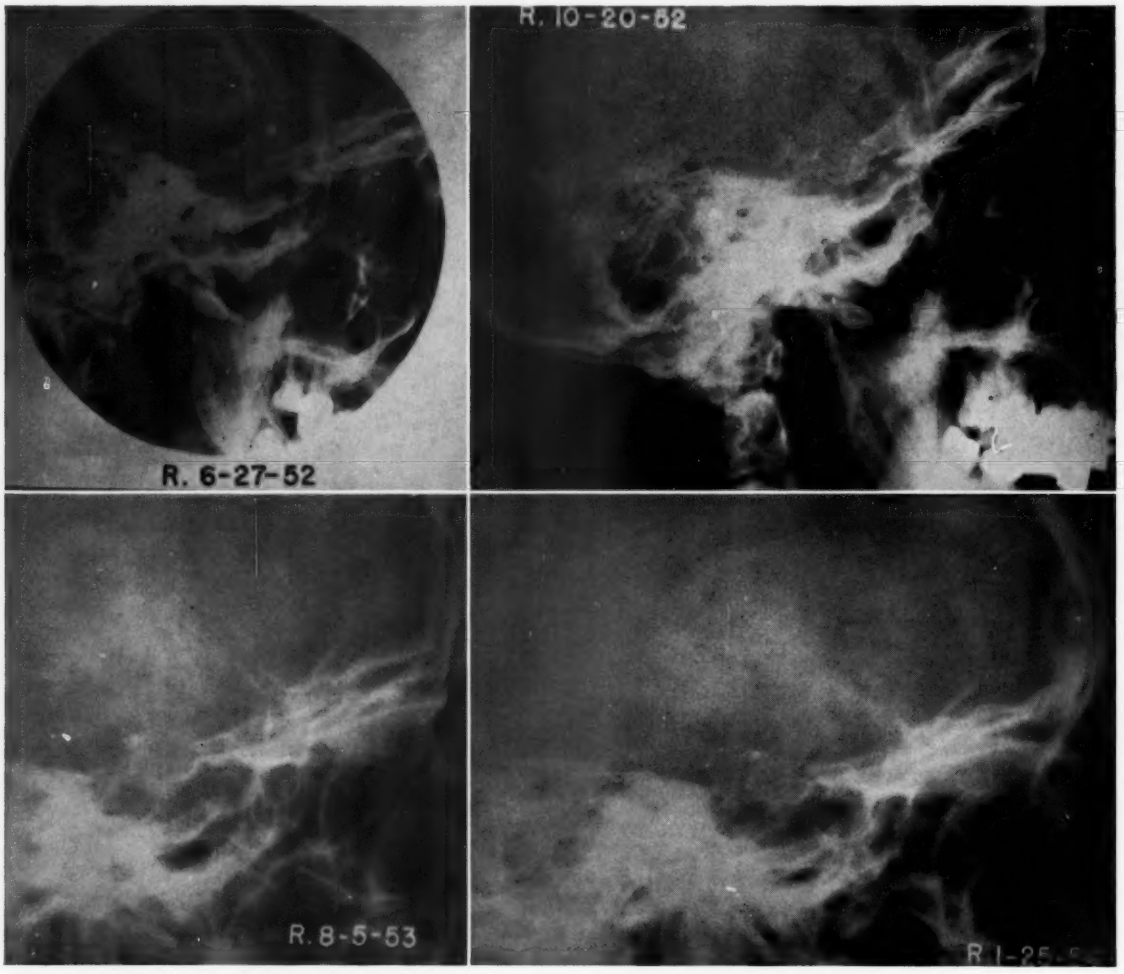

Fig. 12. Follow-up roentgenograms of the same patient as in Figure 11 taken during the ensuing nine months, showing gradual recalcification of the sella turcica and posterior clinoid.

We have had a sufficient number of successful results to encourage us very definitely. However, the dosage must be decidedly above the rather uniformly accepted tumor dose of 6,000 r and it must not be pushed to the point of producing too severe a mucosal reaction (even though postnasal tube feeding is being relied upon).

For example, a man under fifty years, in good general condition had a Grade 2 epidermoid carcinoma of the base of the tonsillar pillar, adjacent tongue and extensive infiltration forward into the floor of the mouth. In addition, he had a 3 cm. lymph node fixed in the under surface of the sternomastoid muscle back of the carotid bulb. He was in domestic service, a combination butler and chauffeur. His employers were relentless in their demands upon him so that he was forced to come late at night for treatment and frequently could not come at all. Over a period of 105 days he received 15,000 gamma r throughout the primary growth and hence a bit more in the enlarged lymph node location. He has had complete regression of one and a half years' duration; the skin does not show evidence of previous treatment and the mucous membrane is moist and comfortable.

Another chauffeur, over sixty years of age but in excellent general health, had, just before the previous case, been treated for a Grade 2 epidermoid carcinoma in the

tonsillar fossa and anterior pillar, primary growth small, not over 3 cm. in diameter, but with a 6 cm. plus fixed mass in the upper third of the sternomastoid muscle. He received over a fifty-seven day period approximately 11,500 gamma r. He lost weight and complained bitterly over difficulty in swallowing. He now has a neck and throat which would defy scar detection by most observers but his throat dryness was annoying for over a year. We cite the case because of the difference in throat symptoms under treatment in the 2 cases, although the real triumph was the complete control of such a sizeable and capsule infiltrated lymph node by external irradiation only.

Along with these 2 cases we must cite another, a woman of just under fifty years of age and in very good general health; and again an epidermoid carcinoma, Grade 2, of the left tonsil and with infiltration into the soft palate for at least 2 cm. In addition she had a 2.5 cm. lymph node under the upper portion of the sternomastoid muscle. Over a fifty-nine day period she received 8,180 gamma r throughout the primary site distribution. She was a complainer by habit and in spite of a very moderate mucous membrane reaction it was difficult to keep her regularly at treatment. What reaction she had subsided quickly and for a time she appeared to be free from growth. However, five months after stopping the beam irradiation at 8,180 gamma r, a small eroded nodule 3 to 4 mm. in diameter was noted on the soft palate at a point corresponding to the most mesial point of original growth extension. Biopsy revealed tumor identical with the original growth. Three radon seeds 1 mc. each and 0.3 mm. gold filter eliminated this nodule and there has been no manifestation of growth for over a year. This little nodule recurring proved with nicety the fact that our original total dose at over 8,000 gamma r still had less than no reserve.

We regard carcinoma of the bladder as one of our most favorable groups, and yet locally we are regarded skeptically by some of our friends. The reason for this was inadequate initial dosage. Two of our initial good cases were undertreated and had to be retreated. Both patients were in good condition generally. One had a very bulky tumor, probably infiltrating the prostate but not outside the bladder confines. He received 7,000 gamma r in eighteen days. Seemingly complete regression had been effected, but within two months there was local bladder reactivation of growth and by way of retreatment he had 5,580 gamma r in a period of eighteen days. Again, tumor regression seemingly complete, next, increasing night frequency and finally a small amount of bleeding and severe local pain. There was still no evidence of tumor recurrence but the bladder was very severely contracted. An exenteration of bladder, prostate and as much of the surrounding tissues as possible was done and the ureters were transplanted into the sigmoid colon.

Fig. 13. Same patient as in Figures 11 and 12. Roentgenogram taken almost two and a half years after initial treatment shows almost complete recalcification of sella turcica.

The other patient had a small localized infiltrating growth. The treatment course was almost identical with the former case. The initial treatment with the Radium Beam was 8,150 gamma r in thirty-seven days and symptoms improved with no cystoscopic evidence of tumor for six months. Then there was recurrence and retreatment with 3,200 gamma r in twelve days and much irritability causing suspension of treatment, followed after a month by

nearly 6,000 r in forty-six days. After several weeks, again increasing symptoms of contracted bladder and local subacute inflammation forced operation for removal of as much tissue as possible and ureteral transplantation. In neither of these cases was any tumor found in the operation specimens.

The bladder and adjacent tissues will tolerate a very large dose in one series—especially if the rectosigmoid is protected or avoided—but retreatment is a practical impossibility because it means essentially two full doses piled one on the other.

Since that time we have repeatedly had no trouble from 10,000 gamma r in a six week period—one field; or 9,000 gamma r through each of two fields in a ten week period.

An off-side observation may be of substantial aid to a group of very painful and largely incapacitated bladder cases, even though they are primarily nonmalignant. In the course of treating a growth in a contracted bladder due to chronic infectious interstitial cystitis with marked bladder wall thickening and contracture, it was noted some months after the treatment that the patient's painful chronic inflammatory disease had been completely relieved. Following this observation several cases of subacute and acute intramural cystitis with spasm and contracture have been treated, with very encouraging results. Our impression is that more prolonged treatment and of smaller single, as well as total dosage intensities, will ultimately prove to be the more satisfactory plan.

We doubt the advisability of offering comment at this stage in the breast field, except to say that if a McWhirter plan is to be followed a quality of radiation of gamma equivalent has certainly more to offer than any axillary conventional high voltage therapy so far reported.

In the field of female pelvic cancer the real contribution from the gamma emitters is by way of control of growth at the lateral borders of the pelvis. It is interesting to observe cases in which the Radium Beam is being used as the sole means of treatment—to prove that it can be done. Practically, however, intracervical and intrauterine radium is a well tried and proven technical procedure that should not be discarded.

SUMMARY

1. Our preliminary experiences of two and a half years using a substantial amount of radium element as a gamma emitter have been very interesting and stimulating. We have seen reactions and results that we had not before experienced. When we couple this adequate quantity of radium element with a Beam Head, such as the one which Dr. Failla has designed and had constructed for us, we are placed in a special position of vantage in that we obtain greatly increased depth doses and with only a limited volume of normal tissue irradiation.

2. Reference to an "adequate" quantity of radium means that we definitely favor the slow delivery in therapy; in the present instance it is 3 gamma r tumor dose per minute at 10 cm. below the skin surface.

3. With this source, and control of the multiple beams, the normal tissue changes in the immediate field of irradiation are much less than with conventional high voltage roentgen radiation.

4. The influence of gamma radiation in bone has a much less damaging effect than with conventional high voltage roentgen radiation, and hence offers the possibility of bone repair after adequate tumor dosage in areas where this prospect was heretofore very doubtful.

5. It is possible that the lesser damage of gamma radiation to soft tissues and bone accounts for the less severe depressing influence on the normal blood forming mechanism of the body.

With adequate intramuscular therapy, while the patient is under daily irradiation, seven days a week, it is seldom necessary to resort to transfusions as an added measure for keeping up a good supporting blood picture.

6. It is our impression that a number of the more resistant types of malignant

growth are now being more favorably influenced by the better quality of radiation and in increasing degree.

7. We believe that with more efficient therapy facilities a revision of the over-all optimum treatment interval may be necessary.

8. We have long felt that the rather universally accepted 6,000 r as an average curative dose of radiation—at the conventional standard high voltage roentgen therapy level—was too low. Our work with the Radium Beam Unit, where skin and surrounding tissue reactions are not a limiting factor, where accuracy of positioning and measurement is assured and after making liberal allowance to cover the controversial equalization of roentgens and gamma roentgens, substantiates the opinion that 6,000 r is too low for a dependable average curative tumor dose.

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New York 19, New York

DISCUSSION

Dr. Edith H. Quimby, New York, New York. I am sure you have all been interested in hearing the first clinical report on this new instrument.

In our day and age one of our favorite expressions is "bigger and better," and unfortunately a good many of us seem to feel that instead of saying "bigger and better" we say "bigger and therefore better." This goes in the field of medicine as in other fields.

We hear that an institution has a bigger x-ray equipment, a bigger source of radiation than any other—cobalt source, multimillion volts, betatron—and the implication is therefore that that place does the better therapy. It may even be stated that therefore this place does the better therapy.

It isn't the place that does the therapy, and it isn't the instrument that does the therapy—it is the radiologist. We can have good therapy without equipment that is too good, but no amount of fancy equipment is going to make up for unimaginative and uninspired treatment planning. However, when there is the combination of a top-flight radiologist, a good radiation physicist, and an excellent radiation source, then we can really expect some results which will be worthwhile. These, I think, we have been hearing about today.

The 50 gram Radium Beam Unit was designed by Dr. Failla to take the best advantage of the biggest amount of radium that had ever been collected in a single unit. Even this biggest amount of radium sounds small to some people who are used to talking now in terms of multicurie cobalt sources, but here again we must say it is the combination of the therapist and the instrument, and not the instrument alone.

The radiation distribution here is essentially the same as would be obtained from horizontal or short axis rotation therapy. This is a rotation therapy scheme which has been very much neglected in this country, probably because of difficulty in setting up the patient and because of difficulty in dosage calculations. However, the clinical evidence that you have heard this morning points out that this scheme is an excellent one for cases which fall into the right category.

It is evident, from looking at the isodose charts and from hearing the clinical results, that the group of patients which will fall into this category is rather surprisingly large.

The dose rate in this particular instrument is low. Dr. Quick was pleased to have it so. He has long advocated a rather slow administration of radiation. Three roentgens per minute at the tumor even with an instrument operating twenty-four hours a day means that not a very large number of patients can be treated.

Dr. Quick was not interested in accumulating statistics. He was interested in making a careful clinical evaluation of a new approach to teleradium therapy. This he has been doing quietly over at least two and a half years, and this he will continue to do.

He has felt that his greatest handicap was not the low dosage rate, but the lack of flexibility of angulation. This beam head has a fixed angle, which means that the focus of all the individual radium beams is at a fixed depth. In the paper he stated that he would rather have several rather small sources with various angles. Of course a variable angle could be set up by fancy engineering, or the same result could be obtained by the use of a single source and rotation of the patient horizontally in the beam, if the factors were properly worked out.

It has long been stated that the advantage of high voltage therapy is that the damage to

the skin is avoided, but that the thing to be watched is damage to deep-seated tissues; and now Dr. Failla, with his engineering, and Dr. Quick, with his medicine, have proved that damage to deep-seated tissues can also be reasonably well avoided with proper care.

The standard rotation therapy techniques, the ones with which most of us are familiar, do spread out the unwanted rays and avoid damage to deep-seated tissues for certain relatively small and centrally located tumors, but for the large, irregular, eccentrically situated mass, standard rotation techniques are not good.

Here we have an approach to a rotation technique or to a distribution by means of multiple beams which lets the radiotherapist attack a new group of tumors with confidence that he can really deliver to them the dose he wants to. As Dr. Quick said in the beginning of the paper, this is an effort to set up a method which other people can then use much more extensively, not an effort to set up a statistically clinical set of data at this time.

I am sure that all of you are just as sorry as I am that Dr. Quick could not come to present this paper himself, and I know also that he was very sorry he could not. Miss Richmond has been associated with the program from before the time the Beam Unit was installed. She has done all of the physical work on it and has been closely associated with Dr. Quick in treatment planning. I am sure that while he isn't here to answer questions, she will be able to give you any information you may want.

Dr. Robert R. Newell, San Francisco, California. I am enthusiastic about the development of multiple beam irradiators. Dr. Quick's instrument is a notable example. But what I wish to discuss here is the dose level that Dr. Quick advises and the impression that radium is much better than roentgen rays for treating cancer.

This last I have called the "paradox of radium." From physical considerations radium gammas are much like roentgen rays. But clinically we nearly all feel that radium is different. I suspect that there is indeed a clinical difference, which lies in the way radium has been used because of its scarcity and because it doesn't give electrical shocks. Radium treatments are usually very slow and irradiate but a small volume.

Small volumes of tissue recover better from radiation damage than large ones because of greater ease of ingrowth of blood vessels from uninjured surroundings. Moreover, roentgen radiation is usually put in through the skin, which becomes denuded after large doses. The resulting infection compounds the damage done by the radiation. For roentgen radiation one usually accepts a tolerable limit of 6,000 r, give or take 1,000 r, and hopes that this will cure cancer and not lead to necrosis of normal tissues. Dr. Quick with his radium irradiator is running the dose up to twice this.

Allowance must be made for the differences in tolerance among different anatomical parts. I think the tongue will recover from twice the dose that the lower lip will bear. Induration and late ulceration occasionally followed our 5,000 r total dose to posterolateral pelvic fields, but the suprapubic field would bear but 3,600 r. More than 6,000 r in the larynx leads to a distressing frequency of intractable perichondritis, and I would expect Dr. Quick's radium beams to produce chondronecrosis if he should run the laryngeal dose up to 10,000 r, just as roentgen radiation would.

In some places, like the head, his radium beams are usable to give doses in the depth which he reports at twice the level I'd think safe with roentgen rays. The availability of such doses will bring many a cancer within reach for hope of cure. If such doses by radium are much better borne than by roentgen rays, it must be because the skin is relatively spared (no complicating infection there), and because the radium gammas, unlike lower energy rays, show but a small disproportion of tissue dose within the bones—and the head is full of bones.

These new instruments let us do more nearly what we would like to do in irradiating tumors beneath the surface. But still our advances rest mostly on the empiricism of clinical experience and clinical judgment.

Miss Richmond (closing). I would like to thank Dr. Quimby and Dr. Newell for their discussion. I agree with Dr. Newell that the problem is probably almost all clinical. There are, however, some physical factors that have to be considered.

I would also like to say, as regards the dosage to the skin surface, that, due to the fact that we have twenty-five beams which do not completely overlap until they reach the focus, at the surface levels at the most five of these beams may have coincided, and therefore the dose at the skin is always considerably less than it is at the focus.

Vol. 74, No. 4

THE USE OF RADIOACTIVE GOLD IN THE TREATMENT OF EFFUSION DUE TO CARCINOMATOSIS OF THE PLEURA AND PERITONEUM*

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INTRODUCTION

THE use of radioactive colloidal gold in the control of ascites and in the treatment of peritoneal masses secondary to ovarian carcinoma was first reported by Müller[5] in 1950; he recorded excellent results in the original 8 cases. Subsequently, however, King *et al.*,[4] Rose *et al.*,[6] Clarke,[2] and Andrews *et al.*[1] documented cases which were not consistently benefited.

This communication is an attempt to evaluate clinically the effects of the administration of intracavitary radioactive gold in 35 patients with pleural and peritoneal metastasis. When viewed as a palliative agent, we found radioactive gold to be helpful in the management of certain cases of fluid collection in serosal cavities secondary to carcinomatous implants. The principal aim is to repress fluid formation so that thoracentesis or paracentesis is either no longer necessary from the time of instillation, or required less frequently.

Radioactive gold is prepared in the nuclear reactor as a result of slow neutron capture by 24 carat gold[197] foil. It has a half life of 2.7 days. A beta particle of 0.98 mev. is emitted, which has a maximum penetration in water of 3.8 mm. In addition, a gamma ray of 0.4 mev. is emitted which accounts for about 5 per cent of the radiation absorbed at the surface. Though a relatively weak gamma ray (half-value layer = 0.33 cm. lead) it does make possible ease in quantitating and localizing the radioactive material. In its colloidal form, gold is supplied as a purple suspension with a specific activity of 20 to 30 mc./ml. The size of the particles range from 0.003 to 0.05 microns. It is therefore readily phagocytized by macrophages. When injected into serosal cavities, the material rather rapidly flocculates on the surfaces of the membranes, though we have found as much as 20 per cent (approximately) to remain in the fluid collections a week after injection. Much of the gold is in the macrophages, which Goldie and Hahn[3] found experimentally to be relatively resistant to this intracellular irradiation.

In the past eighteen months ending March 15, 1953, 35 patients have been treated by the instillation of radioactive gold into the pleural or peritoneal cavities by the Radiologic Service. There were 22 injections into the pleural spaces on 20 different patients. There were 14 cases of carcinomatous ascites in which gold was used. In addition, there were 2 cases of obstructive ascites in which gold was instilled. The distribution of these cases, excluding the obstructive cases, according to site of the primary tumor and location of fluid is set forth in Table 1. Eight of the cases were males; 25 were females.

METHOD

Injection is readily accomplished following fluid removal by a closed system essentially similar to that described by Clarke[2]. To improve distribution of the colloid, the patient is placed in his bed, the foot of which is elevated by shock blocks. Starting with his head low (at the head of the bed), the patient is placed in the following positions for fifteen minutes each: (1) prone, (2) on right side, (3) on left side and (4) supine. At the end of this hour, the patient's position is reversed (head at foot of bed) and he is rotated through the same four positions for the

* From the Departments of Radiology and Surgery of Columbia University, College of Physicians and Surgeons, and the Radiologic and Surgical Service of the Presbyterian Hospital, New York. Presented at the Thirty-fifth Annual Meeting, American Radium Society, St. Louis, Mo., April 20–22, 1953.

TABLE I

DISTRIBUTION OF CASES ACCORDING TO SITE OF THE PRIMARY TUMOR AND LOCATION OF FLUID

Tumor Origin	Peritoneum		Pleura	
	Cases	Favorable Response	Cases	Favorable Response
Breast	2	2	11	9
Ovary	11	7	1	1
Lung			6	
Thyroid			2	2
Colon	1			
Pleura			1	1
Stomach			1	1
Total	14	9	22	14

Eight of the patients were male, 25 were female. One ovarian case had fluid in the chest and abdomen, both successfully treated. The number of favorable responses is also shown.

same periods of time. The shock blocks are then removed and the patient is free to assume any position he wishes. A check of the distribution of the gold following this simple two hour procedure has shown it to be relatively even in all cases.

In order to permit a greater concentration of gold to be in contact with the pleura and to encourage adhesion formation, it is desirable to have the pleural space as free of fluid as possible at the time of instillation of the radioactive material. However, in most patients cough and discomfort in the chest develop after the removal of too much fluid from the pleural space at any one time. To remove as much fluid as possible with the least discomfort to the patient the following procedure is carried out:

A thoracentesis is performed on the day preceding the instillation of gold; codeine sulfate 0.03 gm. by hypodermic is given one-half hour before. Fluid is removed until cough occurs when the patient takes a deep breath. Overnight, the lung is able to readjust to this reduced amount of fluid. At the time the gold is to be administered, fluid is again removed until cough occurs on deep inspiration. An additional 100 cc. may be removed, however, since this quantity will be replaced in the transfer of the gold into the pleural space. Thus removing the fluid in two stages, a greater total quantity may be removed from the patient without discomfort.

DOSAGE

In treating pleural effusions the dose ranged between 21 mc. and 47 mc. The usual dose in a case not suspected of being loculated was 35 mc. Recently the dose has been increased in the patients who have no evidence of loculation, from 35 mc. to 40 mc. In patients in whom pleural loculation is suspected, the dose is usually limited to 25 mc. or less. Most patients with ascites received approximately 100 mc. of gold with a range of 50 to 120 mc. The former amount was used in one instance because no more was available at the time.

DISCUSSION

The results of treatment are itemized in Tables I, II and III. The length of time over which no further tap was required is used as an index of efficacy of treatment. The periods of good, fair and poor results are all necessarily short because in these advanced cases survival is usually measured in months, and in a number of cases in weeks. If a patient died in less than one month, he was placed in a special category because it is felt that he died too soon for gold therapy to be evaluated. If fluid recurred in less than one month with the patient surviving, treatment was rated as a failure. If the need for tapping was not required for a period of between one to two months the result is considered fair. A good result is represented by those cases in which further tapping was not required for two months or more after the instillation of gold.

TABLE II

RESULTS OF TREATMENT OF 22 PLEURAL EFFUSIONS

Pleura—20 Cases—22 Areas

	Areas
No tap required for 2 months or more	8
No tap required for 2 months or more after 3 week tap	4
No tap required for 1 to 2 months	2
Failures	3
Died in less than 1 month	3
Injection into small loculations	2
Total	22

It will be noted that in 4 patients with pleural effusion with ascites a tap was required about three weeks after instillation of the gold. Following this, however, there was a period free of fluid re-accumulation which in the chest cases lasted more than two months. It should not be surprising that such a latent period is found when one considers the delay which occurs between treatment and effect when other forms of radiation are used. In this evaluation, therefore, the initial tap, if performed within three weeks of the instillation of gold, is discounted.

Twenty-two pleural effusions were treated (see Table II). Three patients died in less than one month.

Two of the instillations were made into small, dense walled, loculated cavities. It was not possible for benefit to occur in this instance, since the cavities could not collapse and in any case represented but a small portion of the intrathoracic volume.

Of the 17 remaining cases, 12 required no further tapping for periods of two months or more. Previous to treatment with gold[198], 6 of these patients required thoracenteses at least once a week, 3 required repeated thoracenteses at least once every two weeks, and 3 others repeated taps between four to eight weeks. This is good palliation as far as the repression of pleural fluid is concerned. Two patients were aided to a moderate degree in that the need for tapping the chest was lacking for six weeks after the use of radiogold. Both of these patients had required thoracenteses at less than weekly intervals. One of these, however, soon after this respite, again needed taps at weekly intervals. The other was a case of mesothelioma. The left lung was almost entirely collapsed. It is worthy of note that even in such an unfavorable situation the gold was able to retard the formation of fluid.

It is well known that a lung which has been permitted to be collapsed for any length of time loses its ability to re-expand. The fact that discomfort and dyspnea were relieved for a period of six weeks without further tapping is a good clinical indication of the effectiveness of Au^{198} in controlling fluid formation. Furthermore, it might well be stated at this point that in patients in whom fluid is forming in the pleural cavity, thoracenteses should be done to keep the lung re-expanded. If not, the situation will eventually ensue in which the lung cannot be re-expanded. At such time if the additional factor of pulmonary metastases occurs, the resultant respiratory embarrassment from intrapulmonic and pleural disease may be impossible to manage.

One or two special items in reference to some of these pleural cases points up the areas in which this radioactive substance may be of value. In 1 of the patients, the entire left visceral and parietal pleura was frosted by carcinoma secondary to a gastric tumor. Bloody fluid was present in great quantity, requiring repeated thoracenteses. The patient had marked exertional dyspnea. Following the use of gold, the patient never required another tap, and reported three months later in estimating the amount of benefit which he had received from the treatment that he could now "run for a streetcar." Perhaps small tumor seedlings or thin frosting of tumor on the serosal surfaces might be restricted in their growth by intracavitary radioactive gold. The patient, incidentally, died three months later after three days of difficulty due to cardiac tamponade secondary to the metastatic disease of the pericardium. At

TABLE III

RESULT OF TREATMENT OF 14 CARCINOMATOUS PERITONEAL EFFUSIONS

Peritoneum—14 Cases

	Cases
No tap required for 2 months or more	6
No tap required for 1 to 2 months	1
No tap required for 1 to 2 months after 3 week tap	2
Failures	4
Died in less than 1 month	1
Total	14

autopsy a small pocket of fluid was present in the left pleural spaces containing approximately 500 cc. In the other areas, the visceral and parietal pleura were adherent.

Two of the patients who are listed under the 12 good results are in reality difficult to evaluate. This difficulty arises from the fact that prior to the use of radioactive gold, the patients had experienced a substantial respite in pleural fluid formation without any treatment except repeated thoracenteses over a relatively short period of time. Because of this, it is now the practice to observe the speed with which fluid reforms in the chest or abdomen before advising the use of radioactive gold colloid. If fluid reforms in sufficient quantity to cause symptoms in less than one month, intracavitary gold is recommended. A number of referred cases left untreated have not required thoracenteses in less than two months. Since two months is a relatively long period of time for patients with advanced carcinoma, there need not be many taps in his remaining lifetime. This rule, of course, is altered in the relatively well patient in whom no evidence of disease is found other than in relation to the serosal surfaces. In such a patient the restriction of fluid formation should be attempted even though the need for tapping is infrequent at the outset.

In the 14 abdominal cases (see Table III) 1 of the patients lived less than one month. It is of interest, however, that in this particular case, following an initial tap two weeks after instillation of radiogold, no further fluid formed and was not forming at the time of death. There were 4 absolute failures in this group of 14 cases, however. Three patients required no further tapping for a period of between one to two months except for the initial tap in 2 patients three weeks after the instillation of gold.

In 6 of the patients good palliation resulted. However, in 1 of these the initial injection of gold was followed by little response. A second injection was performed some five months later after which no further paracenteses were required until the time the patient died.

In general, little effect has been seen on abdominal masses. However, in at least 2 of the good palliative results in which both masses and fluid were present, the fluid stopped forming while the masses slowly grew until the patient's death. In these cases the fluid was the item which caused rapid increase in symptoms necessitating repeated paracentesis. Therefore, there can be no question that gold was an aid in the management of these terminal patients.

One patient, who first presented herself for examination over a year ago, deserves special mention. She had been found inoperable because of large abdominal masses with a frozen pelvis secondary to ovarian carcinoma. Fluid was present to a marked degree not only in the abdomen, but also in both pleural spaces. Though postoperative external irradiation was attempted, this was not tolerated by the patient. Following the intra-abdominal instillation of 100 mc. of radioactive gold, the fluid disappeared from both the abdomen and chest. The masses also completely disappeared to clinical examination. Some six months months later, however, a small mass was again felt in the abdomen anterior to the uterus. Because of the remarkable result the question arose as to whether an inoperable ovarian carcinoma had been rendered operable by this intracavitary irradiation. Accordingly, a laparotomy was done. The mass which had been palpated was a combination of omentum adherent to the uterus, and many small cystic carcinomatous masses. This was removed. A number of small cystic carcinomatous masses were also present on the peritoneal surfaces, both parietal and visceral. Two weeks following operation, therefore, a second treatment was carried out in which 119 mc. of radioactive gold was instilled even though no fluid was present. The patient remained well until the last week in March, approximately one year since the

first treatment. At the present time a second mass is found low in the pelvis. No fluid has formed, however. This is the only case in which masses have disappeared. It can perhaps be attributed to the fact that these tumor masses were composed mainly of thin walled cysts, the tumorous lining of which was not beyond the range of the maximum penetration of the beta rays emitted by radioactive gold.

Two patients were treated intraperitoneally whose ascites was not due to peritoneal metastases. These 2 cases are of interest because the idea had been entertained that nonmalignant effusions or peritoneal implantations might respond to Au^{198}. The chylous ascites was due to an obstruction of the thoracic duct by a retroperitoneal mass. No effect in repressing the collection of chylous fluid in the abdomen resulted. The second case was a patient who was erroneously treated for carcinomatosis of the abdomen. In reality cirrhosis of the liver was the cause of the recurrent obstructive ascites. Again, in this instance, no effect in repressing the collection of fluid occurred.

SIDE EFFECTS AND PROTECTION PROBLEMS

Side effects from Au^{198} have been minimal in both incidence and severity.

In 1 patient in whom 47 mc. was instilled, a sterile pleuritis resulted. This patient had all the symptoms of pleural irritation as well as a moderate febrile reaction for a period of six days. Repeated cultures of aspirated fluid were sterile. This patient subsequently showed an excellent response to the Au^{198} therapy. Except for a thoracentesis performed three weeks after instillation of gold, no further fluid removal was required for the remainder of this patient's life (4 months). A second case, in which side effects occurred, received 25 mc. of gold in the right pleural space and 28 mc. in the left. A moderately severe pleural reaction followed each injection. This reaction probably would have been avoided had it been realized that the fluid collections were in very small and loculated cavities. Therefore, for this particular patient the amount of gold instilled was relatively large. However, exceeding the usual dosage of 35 mc. for pleural effusion does not always cause adverse side effects.

For example, 1 patient who had pleural effusion bilaterally was treated with 35 mc. on one side followed two days later by the instillation of 21 mc. on the opposite side. She suffered no ill effects from this dosage and is one of the patients who has remained free of further effusions for a long long period of time (14 months).

Eight of the 16 patients treated for ascites experienced radiation sickness lasting from one to six days characterized by the symptoms of lassitude, anorexia, nausea and in some instances vomiting. In 2 patients signs and symptoms suggesting a chemical peritonitis occurred. In both of these patients an eventual good effect was obtained as far as the repression of fluid formation was concerned.

It is to be noted that no significant exposure occurs to the operators in the transfer of as much as 120 mc. of Au^{198} to the patient.

Nurses were monitored by small ionization chambers placed on their hands and bodies. These nurses, who attended to all the needs of the patient for eight hours immediately following the administration of a 100 to 120 mc. of Au^{198} intraperitoneally, did not receive amounts of radiation approaching daily tolerance levels.

CONCLUSIONS

As a result of the observations on these thirty-five patients, it is concluded that the use of radioactive gold in the treatment of carcinomatosis of the pleural and peritoneal surfaces is purely a palliative procedure directed against the repeated formation of fluid. For this particular purpose in the management of the advanced cancer patient, however, radioactive gold has proved to be of value in over half of

the patients who survived one month or longer. It is our impression that for this limited purpose it is superior to the use of external irradiation. Not only are a larger number of patients benefited, but it is easier to administer and the over-all morbidity is decreased.

Second, it is important to reiterate that radioactive gold cannot be depended upon to decrease the size of abdominal masses. Should abdominal masses be present, especially in the case of ovarian carcinoma, external irradiation should have a fair trial before the patient is given radioactive gold. While it is true that radioactive gold cannot be expected to reduce the size of tumor masses, this does not mean that the annoyance of repeated fluid accumulation cannot be prevented in cases in which tumor masses are also present along with fluid in the abdomen.

Third, before radioactive gold is used, an estimation of the rapidity with which the fluid reforms should be made, especially in advanced cases in relatively poor physical condition. The use of gold is not warranted if a thoracentesis or paracentesis is not required more frequently than once every month.

Finally, Au^{198} failed to control the return of ascites in two patients in whom fluid collection was not due to carcinomatous serosal implantation.

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TREATMENT OF MALIGNANT SEROUS EFFUSIONS WITH RADIOACTIVE COLLOIDAL CHROMIC PHOSPHATE*

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A PRELIMINARY report of our results with the use of radioactive colloidal chromic phosphate in the treatment of serous effusions of the pleural and peritoneal cavities was first presented before the meeting of the Gynecological Section of the California Medical Association in May, 1950.[1] A second report dealing with the use of this material in a larger group of patients was presented by the author before the Sixteenth Meeting of the American College of Surgeons in Los Angeles in January, 1951.[2] The technique was described pictorially in the scientific exhibits of the Clinical Meeting of the American Medical Association in Los Angeles in December, 1951,[3] and the annual convention of the American Medical Association in Chicago in June, 1952[4] and at the American Roentgen Ray Society in Houston, Texas, in September, 1952.[5] This report is an evaluation of the results of the first 50 patients who were treated by this method between 1949 and 1952 and who were followed for a period of six months to three years after treatment.

Clinical results from the use of colloidal radiogold (Au^{198}) in the treatment of serous effusions associated with cancer have been reported by Müller[6] and others. Some radiation hazards and practical problems connected with the intraperitoneal and intrapleural use of radiogold prompted us to search for an equally effective agent which would have a longer physical half-life and thus be easier to keep in supply, would have pure beta radiation and thus require less unwieldy lead shielding for protection and therefore cost less to ship by air freight, would gain Atomic Energy Commission permission to inject on an out-patient basis and thereby cost less to administer to the patient.

When the soluble form of radioactive phosphorus (P^{32}) is converted into the colloidal suspension of chromic phosphate, the radioactive phosphorus retains its radiation characteristics as though it were in the soluble form. Hereafter, in this text, whenever P^{32} is referred to, it should be considered in the form of radioactive colloidal chromic phosphate.

COMPARISON OF RADIATION CHARACTERISTICS OF Au^{198} AND P^{32}

The amount of radiogold ordered often must be larger than the actual need for the patient. A clinic in Los Angeles ordering from Oak Ridge or North Chicago races against time, the physical half-life of Au^{198} being 2.7 days. Some of the isotope inevitably decays in transit. Therefore, the first qualification for another radioactive therapeutic agent is a more favorable physical half-life, such as the 14.3 day half-life of P^{32}.

Beta radiation constitutes 90 to 95 per cent of the effective radiation of Au^{198}. Does the gamma radiation contribute to the clinical effectiveness of radiogold? Only clinical trial could demonstrate this. Radioactive chromic phosphate, with 100 per cent beta radiation, might prove equally efficacious. The cumbersome lead shielding which is required to protect against gamma radiation in Au^{198} can be dispensed with, if radioactive colloidal chromic phosphate can be used instead.

As shown in Table 1, the phosphorus beta ray has a higher energy than the Au^{198}

* Presented by title at the Thirty-fifth Annual Meeting, American Radium Society, St. Louis, Mo., April 20–22, 1953.
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TABLE I

RADIATION CHARACTERISTICS

	Radioactive Colloidal Gold (Au^{198})	Radioactive Colloidal Chromic Phosphate (P^{32})
Physical decay	2.7 days	14.3 days
Gamma dose rate	0.24 mr/hr/mc. at 1 meter 2.4 r/hr/mc. at 1 cm.	None
Beta dose rate	76 rep/gm/uc.	885 rep/gm/uc.
Av. energy beta	0.3 mev.	0.7 mev.
Max. range beta	3.8 mm.	8.0 mm.
Av. range beta	0.7 mm.	2.5 mm.
Particle size	0.003 to 0.007 micron	−1 to 2+microns

beta ray. For example, the beta-ray dose rate for Au^{198} is 76 roentgens equivalent physical (rep) per gram per microcurie destroyed, for P^{32} 885 rep per gram per microcurie destroyed. The average energy beta of Au^{198} is 0.3 million electron volts (mev.), for P^{32} 0.7 mev. The maximum range for Au^{198} is 3.8 millimeters, for P^{32} 8.0 mm. Average ranges are 0.7 mm. for Au^{198} and 2.5 mm. for P^{32}. The higher energy of the phosphorus beta ray may be more advantageous therapeutically. If clinical results from the use of radioactive colloidal chromic phosphate compare favorably with the results from radiogold, the importance of the gamma radiation in Au^{198} would be minimized.

PRACTICAL CONSIDERATIONS

Table II contrasts some practical considerations in the use of Au^{198} and P^{32}. In many clinics only enough radiogold for each individual or each group of cases can be ordered because the rapid physical decay of the isotope (2.7 days half-life) would make its storage for future use impractical. Radioactive colloidal chromic phosphate, on the other hand, can be kept in constant supply because of the longer half-life of P^{32} (14.3 days). If a patient unexpectedly needs treatment, the P^{32} is available without delay. For example, a surgeon finding an inoperable neoplasm may inject the radioactive phosphorus interstitially during the operation.

Lead shielding is the required protection for radiogold. A plastic shield and rubber gloves are adequate for radioactive chromic phosphate. Radiogold must be shipped in a 32 pound lead container. Air freight cost for radioactive chromic phosphate shipments is much less, for it can be shipped in an ordinary tin can.

The expense to the patient is higher for radiogold, because the patient must be hospitalized for this treatment, according to Atomic Energy Commission rules. For intrapleural and intraperitoneal therapy with radioactive chromic phosphate an out-patient technique is practical and permissible. Many patients needing this therapy have already been through expensive surgical and external radiation procedures. The mental depression of the patient and his poor financial condition are characteristic, because of the expense incurred during the chronic illness. The radioactive phosphorus method of treatment is much more economical for the patient.

Radiogold can be stored and prepared only in a suitably shielded area. A shipment of 300 millicuries of Au^{198} raises the radiation background in the laboratory, and this may cause errors in nearby radiation measuring instruments. With radioactive chromic phosphate, this effect is not a problem, since there are no long range gamma rays present to affect radiation instruments.

TABLE II

PRACTICAL CONSIDERATIONS

	Radioactive Colloidal Gold (Au^{198})	Radioactive Colloidal Chromic Phosphate (P^{32})
Supply (half-life)	Order for each patient	Constant supply
Protection (gamma rays)	Lead rubber gloves and lead shield	Rubber gloves and plastic shield
Cost air freight	Lead pot	Tin can with small lead shield
Cost to patient	Material given, 50–160 mc. in hospital	Material given, 5–30 mc. in outpatient department
Facilities	Special space	Any space
Decontamination	Hypochlorite bleach powder	Soap and water
	Storage	
	Effective life 3.9 days	

Radiogold must be handled with complete protection by lead shielding. It can be decontaminated with hypochlorite bleach powder. However, rubber gloves protect the skin sufficiently against radioactive chromic phosphate. Washing off rubber gloves with soap and water usually decontaminates. If P^{32} falls on the floor, soap and water scrubbing decontaminates easily. Use of radioactive colloidal chromic phosphate is practical in the radiation therapy department or in the operating room where the material is removed simply if spilled or dropped. Certain circumstances may indicate that actual storage for physical decay is the best disposal of the waste material. This is not a serious problem for either radiogold or radioactive colloidal chromic phosphate, since the half-life for both isotopes is relatively short.

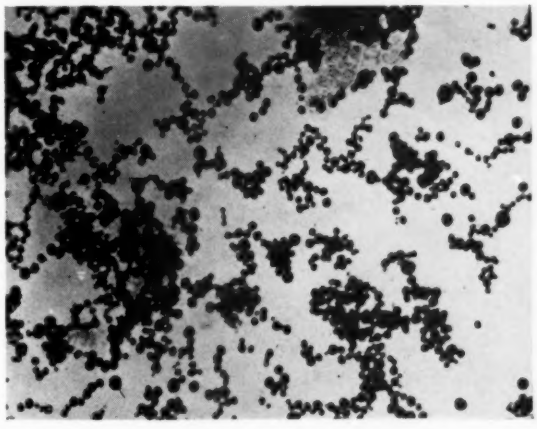

FIG. 1. Electron microscope photograph of particles of radioactive gold (magnification, ×7500).

PREPARATION OF RADIOACTIVE COLLOIDAL CHROMIC PHOSPHATE FOR CLINICAL USE

The preparation of the material and standardization of particle size were a problem at the beginning of our work with chromic phosphate in 1949. We could not obtain it commercially and therefore made our own material according to the method of Jones, Wrobel and Lyons.[7] The greatest difficulty of trying to make colloidal chromic phosphate by simple methods is avoiding a variation in particle size. Recently, Tabern[8] developed a method of making a fairly uniform radioactive colloidal chromic phosphate with a range in particle size from 0.1 to 0.4 micron and reasonably uniform.* The particle size for colloidal radiogold ranges from 0.003 to 0.007 micron (see Table 1).

Figure 1 is an electron microscope photograph of the particles of radioactive colloidal gold, which are fairly uniform in size. Some clumping occurs but not so much as with the original preparation of colloidal chromic phosphate. Figure 2, an electron microscope photograph, shows how much larger the colloidal chromic phosphate

* In the Abbott Laboratories.

Fig. 2. Electron microscope photograph of particles of radioactive colloidal chromic phosphate (magnification, ×6400).

particles are than colloidal gold particles. Large masses are clumps of smaller ones. Figure 3 pictures some material made in Los Angeles. Again, with the electron microscope, the tendency to clumping, which is a definite disadvantage, is demonstrated. Results from a material that clumps badly are not comparable to results from a better material in which the particles are finely distributed in colloidal suspension.

Sherman[9] also had the same difficulty with production of colloidal chromic phosphate in St. Louis. His group in trying to make the material found that the particle size in one batch was different from the size in the next.

Figure 4 is an Abbott Laboratory preparation showing their developments in the preparation of colloidal chromic phosphate. Another problem to be solved was that autoclaved material tended to clump (Fig. 4, *A* and *B*). After Tabern used pectin, he got a much smaller particle size and a nice distribution. But pectin had a proclivity to settle out (Fig. 4*C*). When he tried glucose, results were better. Figure 4*D* shows a fairly typical distribution of the particles in glucose. Figure 4*E* shows the newest chromic phosphate material prepared by Tabern with a fine dispersion of the particles, which measure from 0.1 to 0.4 micron and are reasonably uniform.

Obviously, to compare results from one clinic to another, the physical factors should be defined as they are in external radiation therapy. Uptake of radioactive material in the liver may vary all the way up to 10 per cent, relative to the particle size.

Apparatus for Administration of Radioactive Colloidal Chromic Phosphate

In January, 1949, at the beginning of our work with radiogold, we devised the lead-shielded apparatus, illustrated in Figure 5, with a closed glass cartridge system for the source of isotope supply. (Ampules or syringes filled from a stock bottle at the time of injection in the operating room or laboratory might result in radiation contamination.) Our pattern was the device of the dentist, now long in use, the novocain cartridge. A special lead shielded syringe holds the glass cartridge so that radiogold can be drawn up into the glass cartridge barrel inside the lead syringe. Loading can be checked through a small lead glass shielded window. A plastic syringe for use with radioactive colloidal chromic phosphate was built on the same principle as the lead syringe previously used for radiogold injection. This plastic syringe is

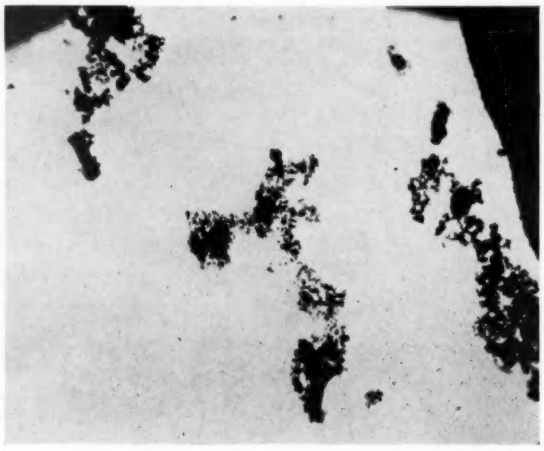

Fig. 3. Radioactive colloidal chromic phosphate showing tendency to clump. (From Tabern.)

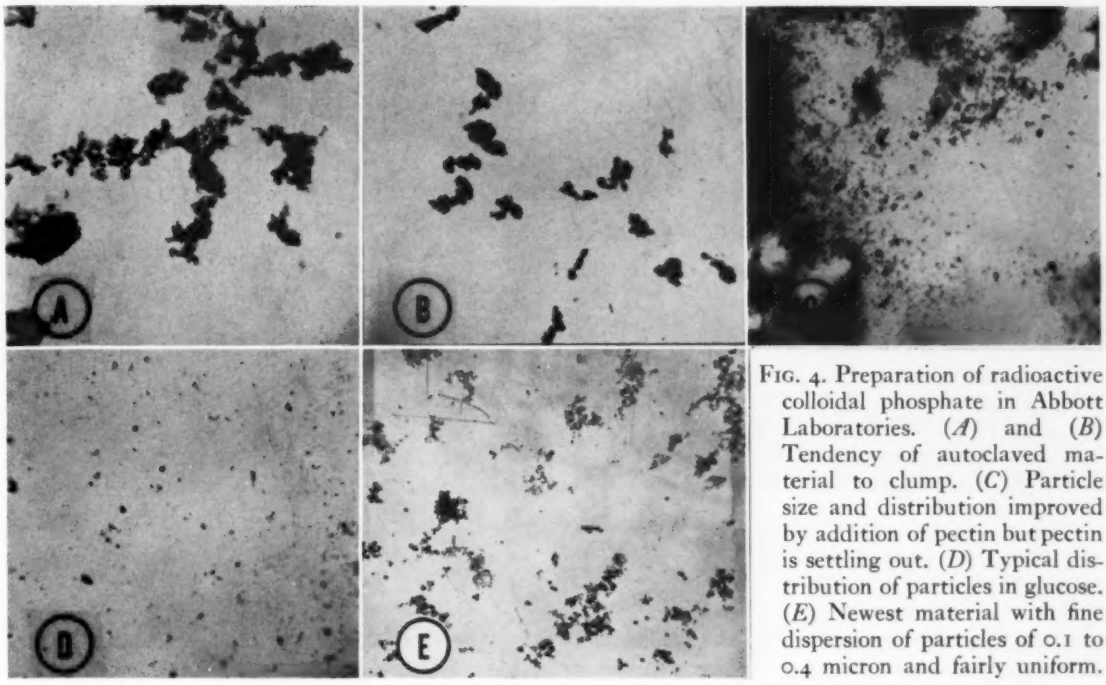

Fig. 4. Preparation of radioactive colloidal phosphate in Abbott Laboratories. (*A*) and (*B*) Tendency of autoclaved material to clump. (*C*) Particle size and distribution improved by addition of pectin but pectin is settling out. (*D*) Typical distribution of particles in glucose. (*E*) Newest material with fine dispersion of particles of 0.1 to 0.4 micron and fairly uniform.

now manufactured, and it is available commercially.* It affords adequate personnel protection for P^{32}.

Figure 6 shows the apparatus used in our clinic prior to the adoption of the new syringe. We had plastic shields made to fit over all standard glass syringes of different sizes. The plastic shield is fastened on with a plastic screw, and it protects against beta radiation coming through the glass syringe. Figure 7 is our new plastic-covered closed-system glass cartridge syringe for use with pure beta radiation isotopes, showing the individual parts.

After the radioactive colloidal chromic phosphate is prepared, it may be drawn up into the individual glass cartridges and stored, ready for use as is necessary for each patient. The cartridges can be stored with a little additional shielding. The concentration of radioactive colloidal chromic phosphate usually is 2 millicuries per cubic centimeter; each cartridge contains 6 mc. of the material. After each injection, the cartridges (which cost only a few cents) can be thrown away.

* Available through the Abbott Laboratories.

INTRAPLEURAL AND INTRAPERITONEAL TREATMENT FOR SEROUS EFFUSIONS IN ADVANCED CANCER

The technique for aspiration of the chest fluid and intrapleural administration of radioactive colloidal chromic phosphate is demonstrated in Figures 8 and 9. Figure 8 demonstrates how the needle is inserted into the pleural cavity in the usual manner. Figure 9 shows the 12 gauge thin-walled needle with the bore of the needle large enough to pass the plastic tubing through it into the pleural cavity, after which the needle is withdrawn over the plastic tubing. This technique minimizes the possibility of the needle tearing the lung and causing a tension pneumothorax. The same technique for the peritoneal cavity is used, and it minimizes the danger of injury to the bowel. Controlled negative pressure assists the collection of the fluid in a commercially available vacuum flask (Fig. 10). The fluid collected can be sent to the laboratory for pathological and bacterial study. After the fluid has been aspirated, the syringe with radioactive colloidal chromic phosphate is attached to the tubing, and

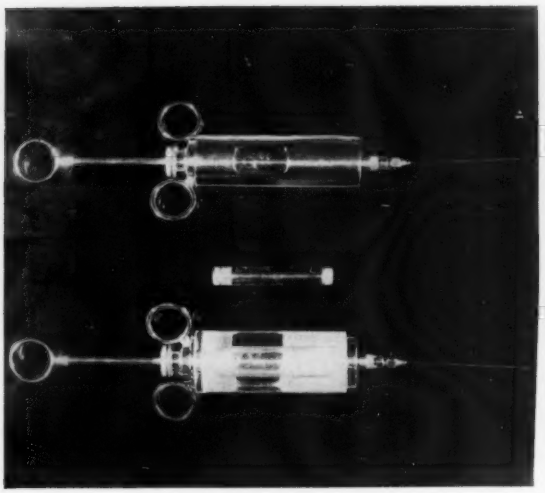

Fig. 5. Apparatus for administration of colloidal radiogold, with lead shielding and closed glass cartridge system.

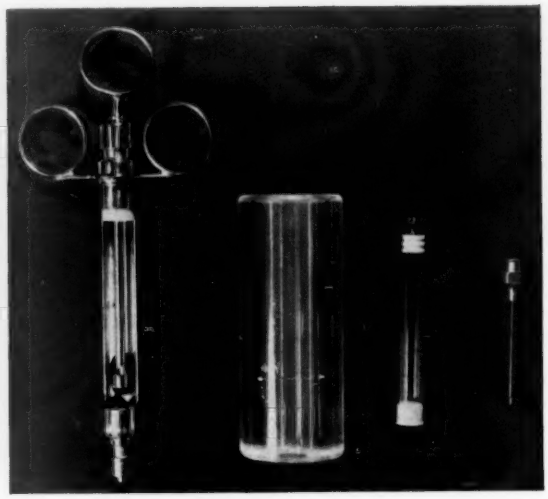

Fig. 7. Special closed-system glass cartridge syringe for use with radioactive colloidal chromic phosphate.

the material is injected (Fig. 11). If the effusion is massive and reaccumulates rapidly, the plastic tubing may be clamped and held in position with a silk suture. This will permit repeating the procedure of drainage and reinjection of the radioactive material at three day intervals. This is possible without loss of the previously injected chromic phosphate because it tends to plate out on the serous surface in seventy-two hours.

The preliminary results of three and a half years of experience with this technique are reported in Table III. In this general clinical evaluation, even the patients who died within a few weeks are included. Many of those patients who were treated with radioactive colloidal chromic phosphate were terminal cases when they received the treatment. To evaluate a method by using it on patients manifestly ready to die is unfair to the method. The treatment is only palliative, however, and patients with advanced metastatic carcinoma are suitable subjects for this type of palliation.

Fig. 6. Apparatus for administration of colloidal radioactive chromic phosphate with plastic shield over ordinary glass syringe.

Fig. 8. Insertion of needle into pleural cavity for intrapleural administration of radioactive colloidal chromic phosphate.

Fig. 9. Technique with thin-walled needle and bore large enough to pass plastic tubing through bore of needle into pleural cavity.

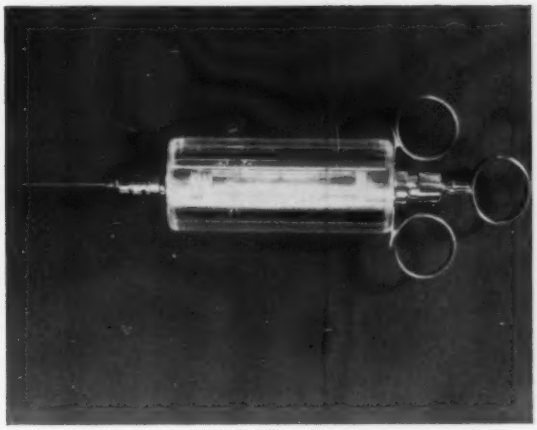

Fig. 11. Special Jaffe syringe (see Fig. 7) completely assembled, with radioactive colloidal chromic phosphate in glass cartridge ready for injection.

The patient who continued to live three years probably did not survive because she had radioactive colloidal chromic phosphate. However, this woman, who had had repeated thoracenteses, has not had pleural effusion since her initial injection in March, 1950, of just 8 mc. of colloidal chromic phosphate. Figure 12 is the roentgenogram of her chest in May, 1950, Metastatic masses near the mediastinum and a large one near the base are shown. We had just withdrawn almost all of the fluid, as we do routinely prior to injection of the isotope. No matter how much fluid one withdraws, even though it may be 3,000 cc., a residue of 300 or 400 cc. usually remains. Figure 13 shows the condition of the same patient in March, 1953. The appearance of the metastatic areas has changed. Possibly some of the shadows that look like masses may be loculated fluid. A metastatic lesion also has developed on the left side of the chest. The patient is still alive, with disease, about three and a half years after her

Fig. 10. Collection of fluid into vacuum flask, using controlled negative pressure.

Fig. 12. Roentgenogram of patient with pleural effusion three months after initial injection of radioactive colloidal chromic phosphate in which metastatic masses near the mediastinum and a large mass near the base can be seen.

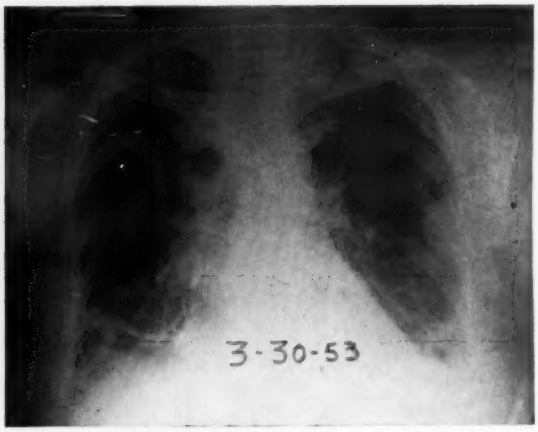

Fig. 13. Roentgenogram of same patient three years later showing change in metastatic areas.

original palliative treatment. This is a good example of the usefulness of radioactive colloidal chromic phosphate.

Results of treating pleural effusions with deep roentgen therapy have not been dependably good, although some patients have responded. Radiation sickness may present a problem when roentgen therapy is administered. With the individual doses of 5 to 7 mc. of chromic phosphate that we use, we have rarely seen radiation sickness. When larger individual doses were used, pain and radiation sickness were observed.

At present we are using 5 mc. of radioactive colloidal chromic phosphate per injection and giving repeated doses to some patients. The quantity we use, 5 mc., is arbitrary, not computed by physical formula. Roughly, the potency of radioactive colloidal chromic phosphate is about ten to twelve times that of radiogold. We have given as much as 30 mc. per injection. With a dose of 10 mc. per injection more patients will have transitory radiation

Table III

Clinical results with radioactive colloidal chromic phosphate in the palliative treatment of advanced carcinoma, intrapleural injection

Pleural Effusion—30 Cases	
1. *Breast Cancer* (7 cases)	
2 Not improved—died in few weeks	
5 Improved—3 living, 3 yr., 1 yr., 6 mo.	
—2 dead, 6 mo., 10 mo.	
2. *Lung cancer* (22 cases)	
7 Not improved—dead	1 wk., 1 wk., 1 mo., 1 mo., 2 mo., 4 mo., 3 mo.
14 Improved—5 living,	3 mo., 9 mo., 4 mo., 9 mo., 6 mo.
—9 dead,	10 mo., 4 mo., 9 mo., 7 mo., 5 mo., 4 mo., 5 mo., 1 yr., 1 yr.
3. *Gastric cancer* (1 case)	
1 Improved—0 living	
1 dead, 3 mo.	
Totals	
10 Not improved = 33⅓%	
20 Improved = 66⅔%	

Table IV

Clinical results with radioactive colloidal chromic phosphate in the palliative treatment of advanced carcinoma, intracavitary injection

Ascites—20 Cases	
1. *Ovarian cancer* (13 cases)	
6 Not improved—6 dead,	1 mo., 3 mo., 1 mo., 1 mo., 4 mo., 1 mo.,
7 Improved—3 living,	4 mo., 1 yr., 17 mo.
4 dead,	13 mo., 7 mo., 1 yr., 13 mo.
2. *Gastric cancer*	
0 Not improved	
3 Improved—0 living	
3 dead,	5 mo., 3 mo., 6 mo.
3. *Lung cancer* (2 cases)	
1 Not improved—1 dead,	4 mo.
1 Improved—1 living,	4 mo.
0 dead	
4. *Lymphosarcoma* (2 cases)	
1 Not improved—1 died,	1 wk.
1 Improved—1 living,	7 mo.
0 dead	
Totals	
8 Not improved = 40%	
12 Improved = 60%	

sickness and some pleuritis or peritonitis, which will last three or four days.

With radioactive colloidal chromic phosphate we began treatment on a low dosage schedule to determine the minimal effective amount. If serous effusion recurred, we repeated the dose every three or four weeks. More recently, we have been treating patients on a three to seven day schedule. Patients with no more fluid after the first injection receive no further treatment. The majority of patients receive two or three injections. Some get only one; others were given as many as six. If the first doses bring no response, at least six repeated doses should be given before considering the case a failure.

Table III shows the results of intrapleural injection with radioactive colloidal chromic phosphate of 22 patients who had primary lung carcinoma with pleural involvement and effusion. The average life expectancy for a patient with inoperable carcinoma of the lung usually is not over a year from the time the diagnosis is made, despite a few exceptionally long survivals. Palliation in 14 out of 22 patients was better than our expectation. The other 8 patients in this group had primary lesions originating in the breast and stomach. Of the 7 breast cases, 5 patients showed improvement. The 1 gastric neoplasm with effusion also showed improvement, but the patient only lived three months after treatment.

In Table III, of 30 cases of pleural effusion, about two-thirds showed improvement.

Results of intraperitoneal injection with radioactive colloidal chromic phosphate in 20 cases of ascites are included in Table IV. Of the 20 cases, 13 were from primary ovarian lesions. The cell type was no prognostication of the response of the patient, which helps to emphasize the point that treatment is given purely for the relief of symptoms. Some of this group who previously had to be tapped from one to three times a week were relieved of the pain and distress associated with ascites and multiple paracenteses. Because some of them have a life expectancy of a year or more, the procedure is worth while.

The 3 gastric patients in Table IV did show some improvement but did not live long. Of the patients with lung cancer, 1 improved slightly. The lymphosarcoma cases were interesting, especially a patient with a retroperitoneal lymphosarcoma that had torn into a thoracic duct so that she required repeated aspirations of chylous ascites. Her condition was deteriorating and her physician was drawing the fluid off as fast as it formed. She had received all the external radiation advisable. Surprisingly, after the third injection of radioactive colloidal chromic phosphate, the chylous ascites changed to clear fluid, and there had been no fluid for seven months at the time the table was made. Now, about ten months after treatment, her general condition has improved.

Of the 20 cases with ascites, detailed in Table IV, 60 per cent improved.

These results compare favorably with the reported results of palliative treatment with radiogold of serous effusions secondary to malignancy. If we were to eliminate the patients in our series who died in the first few months, our over-all results would be better than those reported for radiogold. Obviously, in scoring the objective improvement, the statistical results will suffer, if a number of terminal patients are accepted for treatment. Since radioactive colloidal chromic phosphate produces clinical palliation with results at least as good as those reported for radiogold, we feel that it is far superior, for it has all the advantages and none of the disadvantages.

SUMMARY

1. Radiation characteristics of radiogold and radioactive colloidal chromic phosphate and practical aspects of their use in therapy are compared.

2. Variation in particle size in the preparation of radioactive colloidal chromic phosphate for clinical use, a demonstrable problem, is now under control.

3. A new closed-cartridge system syringe

for the administration of radioactive collodial chromic phosphate is described.

4. Intrapleural injection in 30 patients with advanced carcinoma resulted in palliative improvement in 20, or two-thirds, of the group with pleural effusion.

5. Intraperitoneal injection in 20 patients with advanced carcinoma resulted in palliative improvement in 12, or 60 per cent, of the group with ascites.

6. Gamma radiation in radiogold is not important to therapeutic efficacy in the treatment of serous effusions secondary to cancer.

CONCLUSION

Radioactive colloidal chromic phosphate is a useful palliative agent in therapy for patients with metastatic carcinoma; it is equally as effective as radiogold and more convenient for use in the clinic and operating room.

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PROTECTION OF PERSONNEL DURING ROENTGENOLOGICAL EXAMINATIONS*

By VINCENT W. ARCHER, M.D.
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IT IS now fairly generally accepted that long continued exposure to small doses of radiation may induce leukemia in certain individuals. In 1944, March's[5] article in *Radiology* pointed to this, and in 1946 Ulrich[7] analyzed the obituary notices in the *Journal of the American Medical Association* for the ten year period 1935–1944. His study showed eight times as many deaths from leukemia among those listed as specialists in radiology as would be expected on a statistical basis. In addition, Henshaw[4] almost uniformly produced leukemia in mice by exposure to radiation.

In thinking over this problem, it seemed possible that exposure of parts of the body not covered by the usual protective garments and apparatus might enter into the picture. It has long been held that this action of radiation causing untoward effects on the blood was exposure of the blood-forming portions of our bodies. Undoubtedly this is true in large part, but work done in our laboratory by exposure of circulating blood seemed to indicate that this, too, might play an important role.

All who have treated widely disseminated radiosensitive tumors have noted that masses quite distant from the areas treated frequently have materially decreased in size. We felt that some effect might be carried by the blood stream. With this in mind, in 1935, we dissected the femoral artery and veins in dogs, shielding everything with heavy lead except the vessels, protecting all other tissues, and slipping lead under the vessels. The roentgen tube with an aperture coned down to just the area of vascular exposure was placed almost in contact with the vessels and allowed to operate for several hours, to see what would happen. No untoward general effects were noted and in several weeks the vessels were again dissected and were found to be fibrotic strands, not necrotic as we had anticipated. We then felt that we were ready for a volunteer patient.

Such a patient presented himself with symptoms of intestinal obstruction due to large palpable abdominal masses, and a large fixed mass in his mandibular region. We explained to this man what we wanted to try, and he, being a very sensible person, readily agreed to be a "guinea pig." The radial artery and veins were dissected and treated as we had treated the experimental animals running the tube at 5 ma., 100 kv., for about three hours. Within a few days his symptoms of obstruction disappeared and the mandibular mass decreased to about one-half its former size and became movable. It seemed possible that we had carried some radiation effect, not demonstrable at the time, to distant areas by means of the circulating blood. Just about this time, 1935–1936, the first reports of radioactive isotopes began to appear, and since this was an easier way to do the same thing we were attempting, we discontinued our work. With present-day vastly improved methods of microanalysis of body fluids, we anticipate doing further work along this line in the near future.

In thinking over protective measures against radiation, therefore, the possible effect on circulating blood was considered, as well as the hematopoietic system. All kinds of protective materials for protecting the entire body and the circulating blood were considered, and one by one were discarded. Lead rubber was too cumbersome and heavy and did not lend itself to tailoring in sleeves, and did not fold sufficiently to cover the lower legs. Many

* From the Department of Roentgenology, University of Virginia School of Medicine and Hospital, Charlottesville, Virginia. Presented at the Fifty-fifth Annual Meeting, American Roentgen Ray Society, Washington, D. C., Sept. 21–24, 1954.

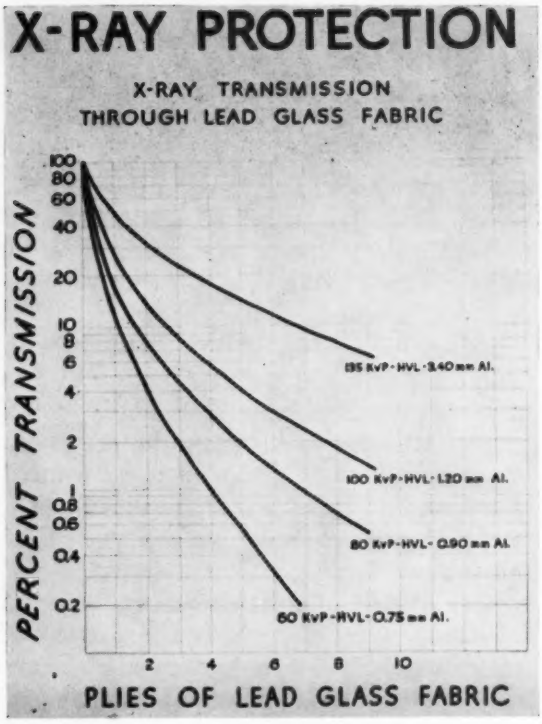


Fig. 1.

impregnated substances were too brittle and would crack on multiple flexing. The thought then occurred, why not make a fabric of spun lead glass? This was produced in the experimental laboratory of the Owens-Corning Fiberglas Company.

The next problem was the percentage transmission of varying voltages through several combinations of the numbers of plies as shown in the first figure (Fig. 1) which is on semilogarithmic chart. It is noted that one thickness will cut out 87 per cent of the radiation at 80 kv. Immediately two other questions arose: (1) What is the voltage equivalent of the scattered radiation from conventional fluoroscopy at 80 kv.? and (2) how much radiation was received over different parts of the body per hour of tube excitation under our own working conditions?

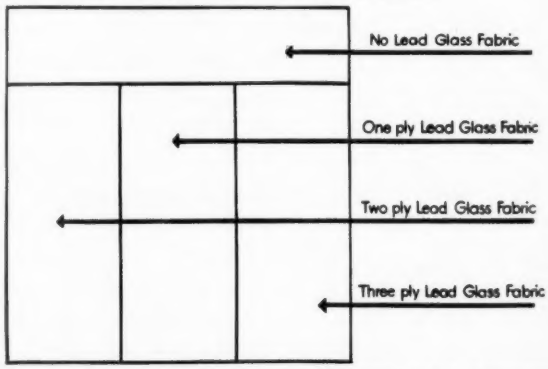
Much to our mutual surprise, Dr. Carl Braestrup discovered on repeated measurements that the scattered radiation from 80 kv. fluoroscopy, using a small shutter image, was approximately equivalent in wavelength to the primary beam, so this question was solved. The amount of radiation received on various portions of the operator was determined by using home-made film packets. These were made up, as shown diagrammatically in Figure 2, using varying thicknesses of the lead glass fabric. Figure 3 shows the location of the badges and the amount of radiation received in the different areas. The larger figure shows the amount transmitted through the several thicknesses of the lead glass fabric. It was noted that for adequate protection of all parts of the body it would not be necessary to have the same thickness throughout the entire garment. By referring again to Figure 3, it is found that one to three plies of the material is all that is necessary to stay well within the 300 milliroentgens per week as recommended by the International Safety Committee. This cuts the weight of the entire garment well below conventional lead rubber aprons

SCATTERED OR STRAY RADIATION RECEIVED BY OPERATOR DURING ONE HOUR FIFTY-NINE MINUTES FORTY-TWO SECONDS ACTIVATION OF FLUOROSCOPIC TUBE

Examinations	
STOMACHS	24
COLONS	15
ESOPHAGUS	4

PACKETS WERE MADE UP AS FOLLOWS :

Kodak Occlusal Superspeed Film partially covered by LEAD GLASS fabric in varying thicknesses with one portion uncovered.



Test films are shown in viewing box below with location on body of operator

Fig. 2

which do not protect the entire body, as well as giving a much better weight distribution since it is belted in at the waist and draped over the shoulders. Another problem was abrasion when it was found that this rather soft fabric would wear out much too fast. This is apparently solved by adding a nylon slip which increases its wearing qualities about fifty times and is readily detachable and washable.

In making our measurements, both with thimble chambers and with badges, it was immediately apparent that different working conditions altered the amount of secondary radiation to a tremendous degree. This is graphically shown in Figure 4, which demonstrates that at least twenty times as much radiation is received at the table edge in horizontal fluoroscopy with the shutter wide open as when there is a 3 by 3 inch screen image. It became evident that to give ample protection without overloading with unnecessary weight, separate measurements would have to be made under each individual's own working conditions. A film monitoring service was contacted to furnish individuals the measurements needed. This is now being used quite extensively and I have had the opportunity to review some of the records. The variation under different individual operating conditions is quite striking, as is shown in Table 1.

These very wide variations intrigued me, and through the courtesy of the monitoring company I obtained the names and addresses of the various individuals who had been measured for exposure. In those in whom the measurements were above the

Table I

1. Right shoulder	20—	330 mr
2. Left shoulder	20—	400 mr
3. Mid abdomen	40—	over 3,000 mr
4. Right forearm	20—	720 mr
5. Left forearm	30—	2,000 mr
6. Right lower leg	0—	230 mr
7. Left lower leg	0—	170 mr
8. Middle of back	0—	180 mr

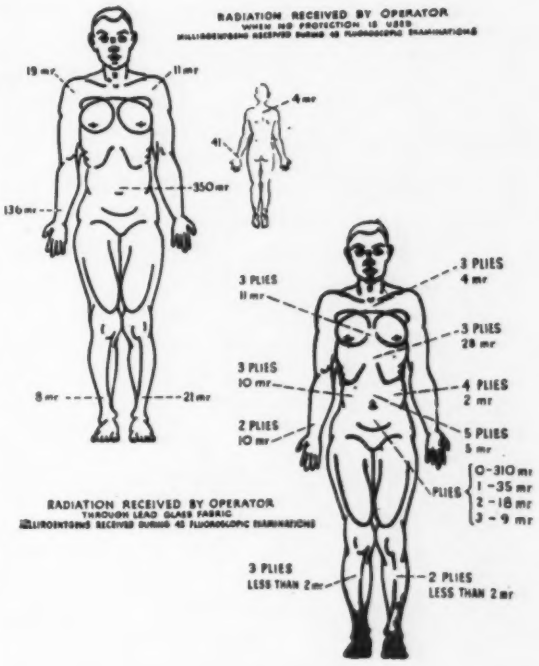


Fig. 3

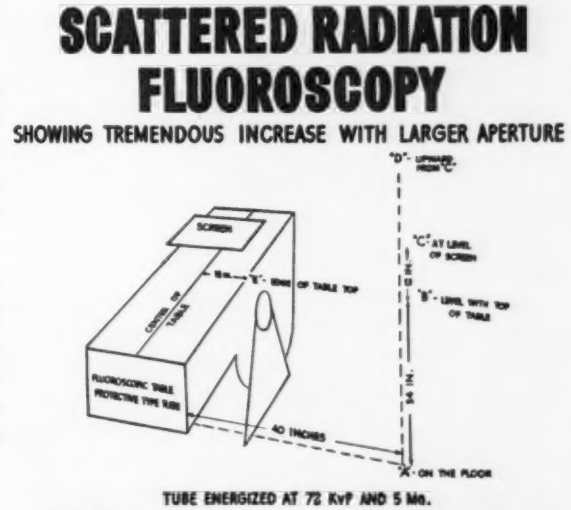

SCATTERED RADIATION
FLUOROSCOPY
SHOWING TREMENDOUS INCREASE WITH LARGER APERTURE
"D"
"C" AT LEVEL OF SCREEN
"B" - LEVEL WITH TOP OF TABLE
SCREEN
CENTER OF TABLE
FLUOROSCOPIC TABLE PROTECTIVE TYPE RUBBER
40 INCHES
"A" - ON THE FLOOR
TUBE ENERGIZED AT 72 KvP AND 5 Ma.
No patient - shutter aperture
Intensity - Milli-roentgens per hour
Closed
Screen image 3 x 3 inches
40 at A, decreasing to 0 above B
50 at A, decreasing to 25 at 'B' and less above 'B'
Fully open
50 at A, increasing to 250 at 'B' and 'C', decreasing above 'C'
PATIENT SUPINE ON TABLE AS FOR BARIUM ENEMA
Shutter aperture
Intensity - Milli-roentgens per hour
Closed
Screen image 3 x 3 inches
10 at A, decreasing to 0 above 'B'
6 at A, increasing to 10 at 'B' and 'C', decreasing toward 'D'; 55 at 'E' (edge of table)
Fully open - no primary passing around patient
10 at A, increasing to 130 at 'B' and C, decreasing toward 'D'
1000 at 'E'

Fig. 4

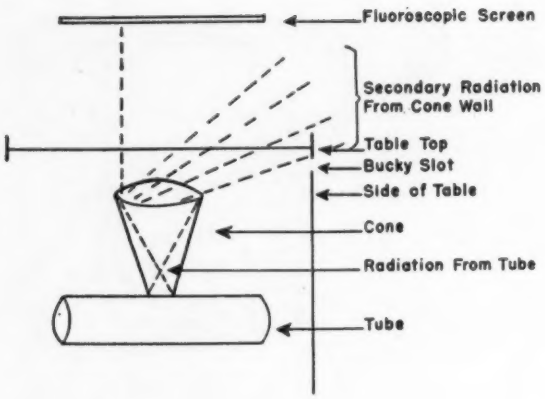


Fig. 5

average a personal letter was written asking the following questions:

1. Hours and minutes that the tube was activated?
2. Do you use a wide or narrow screen image?
3. Is the Bucky tray aperture very wide?
4. Does the fluoroscopic tube cone come close to the table top?
5. How much spot film work do you do?

Parenthetically, regarding the first question of minutes of fluoroscopy, we have come to regard this as quite important and are incorporating a statement of fluoroscopic tube time in every report, *e.g.*, "Time 3½ min." We feel that this is quite a safeguard for many of our patients will report that they have had several stomach examinations elsewhere within a week before coming to us. It is safer to have a record of how much radiation you gave them in case of a cumulative skin reaction, since, according to Donaldson,[2] about 12 per cent of all malpractice suits against physicians are due to skin reaction from fluoroscopy.

A simple self-starting electric clock can be put in the foot switch circuit for about $8.00 and you can record the time the tube was operated, and then state this on the report. In addition the r per minute output of each tube should be calibrated so that the total fluoroscopic radiation received by the patient is recorded permanently.

In answer to the first question as to hours and minutes of tube activation, it is apparent that a relatively small percentage of doctors doing fluoroscopic work have a record of the actual fluoroscopic time. Keeping this record tends to cut down the time used by the operator since it keeps him more "time conscious" as well as providing a record which can be taken into court in the event of a skin reaction resulting in a malpractice suit. I would urge that such time records be kept and made an integral part of every fluoroscopic report.

"Do you use a wide or narrow screen image?" Since it was shown by our measurements that scattered radiation can be increased up to twenty times by using too large shutter apertures, it was not surprising to find that several doctors answering this question admitted that they had been doing this, and a few thanked me for reminding them of this danger. Many fluoroscopists have told me that they like to look at the chest or abdomen as a whole before coning down. I felt the same way, but taught myself to go over the chest or abdomen as I would go over the chest with stethoscope, observing part by part.

"Is the Bucky aperture very wide?" This is particularly important in horizontal fluoroscopy where the operator is standing alongside the table with the abdomen close to the Bucky slot. The metal on the sides of the undersurface of almost all fluoroscopic tables will cut the radiation down markedly. This will be discussed more fully along with the next question.

"Does the fluoroscopic tube cone come close to the table top?" Actually this question could have been worded more clearly by asking "Does the cone come close to the undersurface of the table?" Figure 5 shows diagrammatically how this radiation is produced and how it escapes through the Bucky slot and between the fluoroscopic screen and the table top. It is noted that the nearer the cone is to the undersurface of the table, the less secondary cone radiation will escape. It is also obvious that a narrow Bucky slot will cut down on the radiation striking the abdomen of the operator. The newer equipment

TABLE II

RADIATION RECEIVED BY UROLOGIST
(20 Pyelograms)
Radiation Dosage—Milliroentgens

1	2	3	4	5	6	7	8
Right Shoulder	Left Shoulder	Mid Abdomen	Right Forearm	Left Forearm	Right Lower Leg	Left Lower Leg	Middle of Back
230	220	500	140	260	60	70	140

almost uniformly has protection over this slot.

"How much spot film work do you do?" In answer to this, it was interesting to note that practically all operators having rather high measurements did a considerable amount of spot film work. Excerpts from some of the replies are as follows: "Yes, an average of 16 exposures for each upper G.I. examination." "We use spot films a great deal." "A great deal." From these answers it is apparent that spot films add materially to the amount of secondary radiation. The increase to the mid abdomen is easily understandable. The left arm is on the shutter control in most instances and this increase is also quite apparent. It is obvious that little can be done to control or lessen the radiation when spot film work is done. Protection against it in exposed areas is the only answer.

Another factor, just entering the picture, is higher voltage fluoroscopy with tubes capable of 140 kv. being used. The protection of the lead glass in the fluoroscopic screen should be tested if this higher voltage is used.

So far, only exposure during fluoroscopy has been considered but there are other procedures in which there is an appreciable exposure. One of the measurements reviewed came from a urologist who, in twenty cystoscopies with retrograde pyelograms, received the radiation shown in Table II. This definitely indicates the need for protection if there is a considerable number of retrograde pyelograms done.

In angiocardiography there is a definite exposure. Studies on this were made by Dotter and Steinberg at the New York Hospital and showed measurements ranging from an average of 45–78 mr. Here again the difference in working conditions will alter the readings tremendously.

The same, of course, applies to cerebral angiography.

In cardiac catheterization, the necessity of a fluoroscopic timing device is very apparent. When the catheterization is difficult, time will go by before you know it, and the incorporation of a buzzer or an alarm of some kind, set to go off at a predetermined period of fluoroscopic time, is very desirable. In our own hands this has cut the time in half. This reduces the radiation to the patient as well as to the operator, and it should be remembered that most of these patients usually have had a considerable roentgenologic workup before cardiac catheterization.

Since we are discussing protection, we may as well briefly consider the amount of radiation received by the patient during roentgenographic as well as fluoroscopic procedures, since the effect is cumulative. Measurements make by Handloser and Love at Brookhaven National Laboratory[3] are shown in Table III.

From the foregoing, it is obvious that there are two general methods of operator protection from stray radiation. First, keep down the amount of secondary radiation, and also, protect the fluoroscopist, observer or technician by appropriate measures.

In cutting down the amount of radiation, there are several factors to be considered.

TABLE III

RADIATION RECEIVED BY PATIENT—DIAGNOSTIC PROCEDURES

All Exposures Made with 0.5 mm. Al. as a Filter

Part	Approximate Dose (roentgens)
Chest, posteroanterior	0.05
Chest, posteroanterior (photofluoroscopic x-ray)	0.7 to 1.2
Lumbar spine, anteroposterior	1.5
Lumbar spine, lateral	5.7
Pelvis	1.1
Pregnancy, anteroposterior	3.6
Pregnancy, lateral	9.0
Kidney-ureter-bladder	1.2
Abdomen	1.3
Gastrointestinal series (stomach, PA) per film*	0.65
Gastrointestinal series (total of six films*)	4.0
Gallbladder	0.60
Extremities	0.25
Extremities	1.0
Skull, posteroanterior	1.3
Skull, lateral	1.3
Fluoroscope	0.28/sec.

* Doses for gastrointestinal series do not include the accompanying fluoroscopy. If these figures are kept in mind, the total dosage received by any part of the patient may be readily calculated. Incidentally, it is a good idea to ask patients if they have had roentgen examinations recently, and particularly in case of skull examination, to find out the approximate number of exposures.

The design of the fluoroscope is of importance. As has been mentioned, decreasing the distance of the fluoroscopic tube cone from the undersurface of the table top will be of aid. Either decreasing the width of the Bucky slot or covering it will also help. Hanging lead rubber or other protective material from the edge of the screen, particularly in horizontal work, will aid very materially. The position of the control handle of the fluoroscopic shutter keeps down exposure on the hand and arm used to operate the shutter. A control handle at the edge of the fluoroscope exposes the arm and hand to secondary radiation coming from the patient, whereas a screen mounted handle largely eliminates this, since the arm and hand are largely protected by the lead glass screen. The area immediately behind the screen is the safest place in the room. In our test measurements we were unable to detect any measurable radiation on the head directly behind the screen. Another quite important method of cutting down radiation both to the patient and operator is to use 2–3 mm. of aluminum for fluoroscopic tube filter. Morgan[6] in the last few years has shown that increasing tube filtration even up to 2–3 mm. of aluminum does not appreciably decrease the image brilliance but cuts down radiation very materially. Few fluoroscopic units come factory equipped with more than 0.5 mm. and never more than 1 mm. Of course, as has been mentioned, the size of the screen image is of the utmost importance in determining stray radiation. Decreasing tube time to a minimum also will help. One can form just as good an opinion with intermittent tube excitation as with constant tube exposure.

After all measures to control radiation emanating from the machine or patient have been taken, there will still be a lot of radiation against which those in the room must be protected. The next question is, how much protection is needed? Of course, there is a limit to which these protective measures can be taken. If the protective devices are too cumbersome, heavy or uncomfortable, people just will not use them. Lead glass fabric seems to satisfy these requirements. I have tried to emphasize the fact that there is a great variation in the amount of radiation received over the same areas under differing working habits and equipment. The only intelligent way to estimate protection needed is to make measurements over exposed areas, the easiest way being film badges. After getting these readings, what amount of protection should one use, or, in other words, what is the tolerance dose? This next statement sounds a bit iconoclastic. Personally, I do not know what the tolerance dose should be. Most of us recall when the tolerance dose as determined by the International Safety Committee was 600 milliroentgens per week. Within the

last few years this same committee has dropped it to 300 mr and in Sweden the tolerance dose is 100 mr. What will future thinking be? It takes many years to determine the cumulative effects of minute doses, so I personally like to add a good wide margin of safety, perhaps 500–1,000 per cent, cutting down the radiation to any part of the body and the circulating blood to a minimum.

SUMMARY

1. There seems to be a causative relationship between exposure to continued small doses of radiation and leukemia.

2. Possibly exposure of circulating blood enters into this picture.

3. Exposure to scattered radiation may be minimized by (a) reducing the screen image to a minimum; (b) proper design of fluoroscopic equipment including added filtration; (c) care in spot film work, and (d) protection of the exposed portions of the body with adequate but not unnecessary protective covering.

4. Fluoroscopic tube time should be recorded on the patient's report.

University of Virginia Hospital
University, Virginia

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DISCUSSION

Dr. Lauriston S. Taylor, Washington, D. C. I am sure that we have all both enjoyed and appreciated the presentation that Dr. Archer has just given to us. His presentation touches rather closely one which is very near to my own heart, and one which I am beginning to think of as what we would call "systems analysis." If one designs an automobile, he may be concerned with the front spring. But certainly he is not going to put a front spring in the car without giving some thought to the rear spring, or how much load the car is going to have to carry, and how heavy the engine is, and so on.

In the past there has been too great a tendency in the whole field of radiation protection to consider one facet at a time. One perhaps considers the hands so we have lead rubber gloves. One thinks of the body, and we have rubber aprons. But all too frequently we fail to see the entire radiation exposure picture.

I think Dr. Archer's approach to the tailor-made gown, or, you might say, individual consideration of each problem, is an excellent one, at least within limits. It takes a little time and thought on the part of the wearer and user; but this, in itself, as Dr. Archer has emphasized, is a desirable feature. It causes the radiologist to have an increased consciousness of the problem of radiation protection, and this leads to doing something about it.

I suspect it will be found that in most instances we will discover that there is a fairly standardized pattern of required protection. On the other hand, there are certainly going to be special instances where unsuspected radiation will be present. Dr. Archer has reported rather briefly on a number of surveys which he has made and on which he now has some factual data, particularly relative to the exposure of different parts of the body. This is particularly important as a starting point in the whole problem of radiation protection, and I might say that the National Committee on Radiation Protection will study Dr. Archer's data with a great deal of interest.

In connection with our program at the National Bureau of Standards, we have been seeking similar data for purposes of guidance in the preparation of our protection handbooks. In this we have not been concerning ourselves as much with the individual operator as we have been with what might be termed the "radiation atmosphere" in the rooms. To this end we have secured the cooperation of a number of hospitals and radiologists in the city and

have been determining the radiation levels under normal operating conditions for a wide variety of circumstances.

While in many instances there have been indications that we are overprotecting ourselves, there are also very definite indications that at times we are underprotecting ourselves. In general, we would prefer to overprotect; on the other hand, overprotection is costly.

I would like to refer to one point that Dr. Archer touched on—namely, the effect of radiation on circulating blood. In both our national and international recommendations we allow approximately five times the exposure to the hands, forearms, feet, legs, as compared with the whole body itself. This is based, primarily, on the superficial damage to the limbs themselves.

One is led to believe that if we take advantage of these higher levels we might lighten up the protection around the arms and legs. On the other hand, if it is proven that the exposure of the circulating blood is one of the limiting factors, then I think we have to reconsider this problem.

I was also particularly impressed by Dr. Archer's recommendations about the timing of operations. I think that just to make the fluoroscopist time-conscious is a worthwhile end in itself. I am sure that if he is time-conscious, and if he appreciates the fact that unnecessary exposure can harm him, he will find ways to substantially reduce the radiation to himself. The keeping of time records will further improve his time-consciousness.

Dr. Archer mentioned particular sources of radiation leakage, such as the Bucky slot, and the leakage effected by the gap between the cone and the under side of the table. There are various conditions, of which these are two good examples, where either operational or equipmental situations can cause more or less stray radiation to reach the doctor. Knowledge of these facts should encourage the radiologist to ascertain that these sources of radiation do or do not exist. I believe the average radiologist will be surprised to find a large number of sources of stray radiation, some of them due to his operational procedure, some due to the type of equipment he has, but in any case sources which, with a little thought and effort, can be easily eliminated.

I would like to express the hope that Dr. Archer and his people will strenuously pursue this line of activity that they have been engaged in. One of our greatest sources of radiation damage probably is in the fluoroscopic area, and the work Dr. Archer is doing will certainly provide us with much of the education we need to reduce it.

Dr. W. Edward Chamberlain, Philadelphia, Pennsylvania. I think everyone realizes that this is not the first time that Dr. Archer and his group have made a contribution to this very important subject of protection in diagnostic procedures.

I would like to mention one factor which he has not emphasized, and that is the value of increasing the speed of the roentgenographic film. It is obvious that the figures he gave on that table, which you may remember showed about 5.7 r as the dose the patient's skin gets for a lateral lumbar spine, and approximately 9 r for the dose that the patient's skin gets when a pregnancy lateral is produced, or something of that sort—those figures would all be cut in half if the roentgen film were twice as fast.

It is not difficult to make your roentgen film about twice as fast as it is today. We find that whenever figures are brought out for exposures to skin, and when we compare them with our own experience, they are about twice as high as we have obtained in considerable studies, and I think it is because we are using a film that is faster (as far as I know) than other radiologists are using.

When we increase the processing time, the developer time of one of our films, by one minute, we get no greater density than we get with our standard developing time. Furthermore, we process our films in a developer at 72° instead of 68°. By choosing the developer, and with the help of Dr. Henny, the head of our Department of Medical Physics, we have done very exhaustive studies along these lines; and by studying the developer and comparing various developers, by increasing the temperature to the time where you get maximum contrast and maximum speed as a result in the given film you have selected, by trying various chemical formulas of the developer, you can arrive at the point where you are getting complete processing; at least as far as we can find out we haven't found any way to increase the speed of the film any further.

It takes about 0.0004 r, 0.4 milliroentgen, to

get density 1.5 on a film processed the way we process it. That means we have a very fast film.

That of course cuts down the exposure to the room, and it cuts down the x-ray atmosphere in proportion.

Dr. Archer spoke of fluoroscopy versus spot films—the amount of exposure produced by spot films. By using these fast films that we have access to because of the way we process our films, and making quite a large series of measurements, we arrived at an average figure like this: Each spot film on the average gave as much scattered radiation to the room, gave the various monitoring devices on the fluoroscopist the same degree of roentgen-ray exposure, that six seconds of fluoroscopy produced. Obviously, it varies all the way from one second up to twenty or more seconds, according to the duration of the spot film exposures.

We usually do not change our fluoroscopic settings with different thicknesses of patients. Some do. We have established 85 kv., 3 milliamperes as factors for our fluoroscopic beam. It is 3 milliamperes; a four-valve rectified tube with long cables (and our cables are very long) does give constant potential.

With that fluoroscopic setting remaining fixed during our fluoroscopic procedures, we find that the average spot film exposure gives the same exposure to the operator, and therefore of course to the patient, as would six seconds of fluoroscopy, which seems to us to indicate that since the fluoroscope is usually turned off for at least six seconds between spot film exposure and fluoroscopy, or for the duration of the spot film procedure, the chances are that taking spot films does not change the exposure to the operator at all.

That may come as a surprise, Dr. Archer, but we vary from patient to patient and we arrived at that figure by careful measurements.

I want to comment about blood stream therapy. I am sorry I can't cite the article at this moment. A very exhaustive piece of work was done on this many years ago—in the 1920s, I believe. The blood was let out of the body of various animals and back into the body through glass tubing which had been lined with paraffin so that the blood stream could go in large amounts through the tube, which was then irradiated in various degrees without any radiation of any part of the flesh of the animal. The precautions to prevent any roentgen-ray exposure to the animals while irradiating the blood stream very extensively were very much emphasized in this experiment.

The doses given to the circulating blood were extremely high—simply tremendous. It was perfectly amazing that no clinical effect could be observed in those animals.

This experiment was accompanied by another very interesting experiment. The general idea was this: When the spleen is irradiated, how much of the effect is due to irradiation of the circulating blood? Everyone knows that you get a more profound effect on the blood picture with irradiation of the spleen than in irradiation of any other organ in the body. That has been shown experimentally by ourselves and by a great many others.

The spleen was extraperitonealized in these experimental animals and was given a pedicle. It was given a skin closure but it was taken out of the abdomen and given a pedicle. Then the animal was wrapped in lead and the spleen was irradiated. The same profound effects on the blood picture were obtained as would be obtained in the event the spleen had been inside the body.

The pedicle was clamped and the spleen was irradiated, and naturally there was no circulation of blood through the spleen during the next experiment. Then, when the irradiation was completed, the pedicle still being clamped, there had been no effect on the animal's blood picture. But as soon as that pedicle was unclamped and the spleen was put into the circulation again, the profound effects upon the blood picture took place, showing that something had been stored up in the spleen in the way of an irradiation effect which then proceeded to produce its effect on the blood picture.

Dr. Robert R. Newell, San Francisco, California. Dr. Archer did not cite the well known fact that radiologists develop ten times the leukemia that the rest of the doctors do. I think we all agree that the fluoroscopic room is the radiologists' big hazard. However, I am surprised to hear that Dr. Archer estimates the dosage to the skin as the danger.

About suits: I do know that the high cost of insurance is not due to the diagnostic radiologist but to therapy. I have never seen a skin erythema that was produced by radiologists in ordinary routine fluoroscopy. I didn't think that was the danger. I thought it was the total

body irradiation. Any amount of radiation is harmful, and we no longer say "tolerance" dose, but rather "permissible" dose.

The principal thing is to keep a sense of balance and not pay attention to small details which add little to the danger while they distract our attention from the big things. Dr. Archer tells how much radiation the forearm gets. But the volume of the forearm is small compared to the abdomen, and the sensitivity of the forearm is small compared to the abdomen. Roughly speaking, I don't care about the irradiation of the forearm, but I do care powerfully about the irradiation of the abdomen.

To record the time in hours, minutes and seconds is my idea of a total lack of a sense of humor. The seconds aren't very important compared to the hours, and you can't tell by the total time how large an area was being irradiated. The really dangerous bad habit on the part of the fluoroscopist is to use an unnecessarily large area. Neither does the record of time tell whether the man was using a large or a small amount of current.

I believe that radiologists will be more willing to use low milliamperage routinely if they have immediately available a foot switch to increase the brightness of the image when they must see sharply for a moment.

It would be nice if we had a throttle as on an automobile, so we could tour slowly when we want to take it easy, and then, when we have to go fast, step on it. Maybe a better comparison is the high and low beam on the headlight so that you can run on the low beam except in the moments when you have to see sharply, and then you can step on the high beam.

I thoroughly agree with the buzzer. I think the radiologist would be very well advised to get himself reminded whenever fluoroscopic times "on" add up to, say, two minutes; then have to reset the timer.

I agree with the matter of overprotection. The trouble with overprotection isn't that it is costly—the trouble with overprotection, particularly in regard to aprons and gloves, is that it results in no protection. If it is inconvenient or too hot, then the heavy apron is worn on the hook instead of on the radiologist.

There is another way to reduce the total exposure, and that is to use higher voltage, because a smaller number of roentgens will give you light on the screen or a picture on the film with less total exposure. It does increase the scatter to use higher voltage, but you have a large net gain in light for the same radiation hazard.

We had better move fast and get safe habits before everybody gets an image amplifier and begins to think that because he uses only 1 milliampere he doesn't have to pay any attention to safety, and then forgets all about it. Let's get our discipline learned quickly while we must.

Dr. F. E. Templeton, Seattle, Washington. Yesterday in the instruction course I presented evidence concerning protection on the spot machine. I will not go into the figures, but I think they point out that spot filming does not increase the exposure to the operator very much.

It can be shown that if one uses a field not larger than 4 by 5 inches, makes an average exposure of 0.2 second, takes an average of ten spot exposures per patient, does ten patients a morning six days a week, he will increase his exposure by only 13 milliroentgens a week. The figure is obtained by measuring the point of maximum intensity on the examiner at the margin of the screen using a 160 pound patient. Parts of the body protected by lead coverings or at greater distances receive considerably less exposure.

Dr. Archer (closing). I will take just a moment to talk about one or two things that were brought out.

First, as to the spot films, all I know is what I see in the papers, these records came in, and I wrote back to the individuals with the high measurements. Those that had high measurements, well above the average, almost uniformly, almost 100 per cent, did spot film work.

Now, it is perfectly obvious that all people doing spot film work are not as cautious in their spot film work as Dr. Chamberlain and his group, and Dr. Templeton and his group, so I think that this must enter into the picture.

Certainly I wish to thank the discussants for bringing out many of the points which I had not considered, and for amplifying some of the points that I did not have time to cover.

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COMPARATIVE EFFECTIVENESS OF ROENTGEN RAYS OF 124 KV. AND 50 MEV. ON HABROBRACON EGGS TREATED IN FIRST MEIOTIC METAPHASE*

By GERTRUDE HEIDENTHAL,[1] LEONARD B. CLARK,[2] *and* JOHN W. GOWEN[3]

I. INTRODUCTION

THE invention of the betatron by Kerst[12,13] led to the practical possibility of using roentgen rays of very high energy levels in medical practice. The special value of this type of radiation as compared to that produced by conventional machines of low voltage has been considered largely in terms of depth dose effects. With low voltages, ionization is at a maximum within the surface layers of cells; below this level it drops off exponentially with depth. At very high voltages, the curve is not exponential, but rises to a peak and then decreases. The exact shape of the curve depends upon the voltage of the machine. By suitable manipulation of equipment ionization can be concentrated on malignant tissue at any depth chosen and the hazard of radiation damage to surrounding tissue can to some extent be controlled (Charlton and Breed[1]).

Consideration has also been given to problems related less directly to depth dose. If, for example, the distribution of ionizations in samples of a given kind of cell or of small volumes of tissue were to be kept as nearly similar as possible, how would the biological effectiveness of the high and low voltage radiations compare? A wide difference in wavelengths, as between 124 kv. and 50 mev. roentgen rays, makes a difference in the method by which ionizations are produced: by Compton and photoelectric effects at low voltage, and by pair production at high voltages. Does difference in wavelength lead to a difference in biological effectiveness even though there is a large component of the long wavelengths in the radiation delivered by the high voltage machine? The answer to this question is quite obviously associated with the problem of dosimetry in medical practice.

To point out the desirability of evaluating the biological effectiveness of the very high roentgen-ray energies is really only to emphasize the thought of others.[1,2,19] Translated into medical practice, biological effectiveness becomes therapeutic efficiency. A number of authors have reported their work on comparisons between effectiveness of high and low energy radiations, but their data appear to lead to conflicting conclusions. Investigations by Chase, Quastler and Skaggs[2] on decoloration of mouse hair, and by Luce, Quastler and Skaggs[16] on sex-linked recessive lethals in Drosophila have been interpreted to mean that high voltage radiations are only about 70 per cent as effective as those produced by conventional, low voltage machines. Confirmatory data for the lower efficiency of radiations from a 23 mev. betatron in inducing recessive lethals has been reported by Regehr, Arnason and Johns.[18] Studies of four strains of yeast by Ting, Chinn and Johns[20] have shown that the ratio of effectiveness for the 50 per cent lethal dose, when 200 kv. and 23.5 mev. radiations are compared, varies between 0.67 for *T. cremoris* and 0.85 for *C. krusei*. Harvey, Haas and Laughlin[8,9,10] say, as a result of their clinical experience, that greater quan-

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tities of measured roentgens are required from the betatron than from machines of low voltage, to produce equivalent effects in tissue. On the other hand, Clark and Sykowski[3] have reported, as a result of their work on the induction of lens opacities in mice, that there was no difference in the effectiveness of 124 kv. and 50 mev. radiations. These authors also claim that other studies at the Union College Laboratory support the same conclusion. Further evidence for the equivalence of biological effectiveness is to be found in the investigations of Fritz-Niggli.[4] Timed embryonic stages of Drosophila were exposed to radiation either from a 180 kv. machine or a 31 mev. betatron. Dose-action curves have indicated no statistically significant differences in effectiveness as judged by capacity of the eggs to hatch after treatment.

It is apparent from the above that the answer to the question of the comparative effectiveness of radiations from high and low voltage roentgen-ray machines is not clear. The purpose of the investigations reported in the following pages is to contribute further data and interpretation in connection with this problem.

II. MATERIALS AND METHODS

The Test Material. A relatively large body of evidence from the work of Whiting[21,22,23,24,25] on the effects of low voltage roentgen rays on the eggs of Habrobracon, a small parasitic wasp, suggested that these eggs might provide good test material for comparing the effectiveness of low and high voltage radiations. In reviewing the basis for the methods used it will be necessary to give a brief description of some of the special features concerned with the reproductive processes. Habrobracon is capable of natural parthenogenesis. Virgin females lay haploid eggs on the host caterpillar of a moth, *Ephestia kuehniella* Zeller, and these unfertilized eggs develop into males. If, however, the females are mated, about two-thirds of the eggs are fertilized and these develop into females. As a rule, then, the sex ratio of progeny of a mated female is about two females to one male. Eggs develop within the four ovarioles, where meiosis progresses up to and including first meiotic metaphase. First and second polar bodies are formed only after the eggs are laid. It is possible, in Habrobracon, to force the storage of eggs in first meiotic metaphase, within the female, by removing caterpillars from the vials in which the wasps live, since oviposition never occurs except on the natural host. If egg laying is prevented in this way for twelve hours or more, up to 20 eggs in first meiotic metaphase accumulate at the distal end of the reproductive tract ready to be laid. Later, when females are placed with caterpillars, oviposition occurs; three polar bodies form, cleavage and later development ensue even though the eggs have not been fertilized.

It follows from the above that one could collect virgins, force them to store eggs in first meiotic metaphase and then irradiate the eggs by exposing groups of females to the radiations. Whiting has shown that all eggs laid during the first six hours after treatment are eggs which had been treated in first meiotic metaphase. Her data also show that a proportion of the eggs fail to hatch as larvae and that the percentage of dead eggs is related to the dosage. The dose action curve is exponential with LD_{50} at approximately 400 r. Whiting's method is advantageous in that it permits study of eggs which are known to have been treated in a cytologically uniform stage.

In the work reported here, virgins of stock No. 33, a wild-type stock which had been highly selected for egg viability, were fed and restrained from oviposition overnight. Then, groups of virgins were treated with either high or low voltage radiations. Each female was placed with a caterpillar and allowed to lay eggs for six hours, at 30° C. At the end of this period, females were killed, eggs were counted and the cultures returned to the incubator. Thirty-six hours later records were made of dead eggs and hatched larvae. This time interval is more than sufficient to allow all viable eggs to hatch.

Roentgen-Ray Machines and Their Use. Low voltage roentgen rays were delivered by a conventional kx-4 roentgen-ray machine owned by Union College. The conditions of irradiation were kept as constant as possible: 124 kv., 10 ma., target-sample distance 33.9 cm., 102 r per minute, no filter except that inherent in the tube. Time of treatment was varied in accordance with dosage desired. The dosage range extended from 100 r to 1,750 r.

High voltage roentgen radiation was delivered by the 50 mev. machine at the General Electric Research Laboratory in Schenectady, New York. Irradiations were carried out in a phantom 14 by 17 by 14 inches deep consisting of $\frac{1}{4}$ inch thick sheets of masonite (density 1.08) stacked in a holder and clamped together by levers at the back end of the framework, which was made entirely of wood. The face of the phantom was carefully lined up so that the axis of the roentgen-ray beam was along the center line of the phantom as determined photographically. The distance from the face of the phantom to the target was 2 meters. Since the electrons are contracted to the target, which is located near the inner wall of the vacuum chamber, there is no evidence for electron contamination of the roentgen-ray beam in the phantom.

The dosage calibrations were made by inserting a standard Victoreen thimble chamber in a hole in the phantom just large enough to accommodate the thimble, and locating it so that the center of the thimble chamber was in the beam axis. The reading of the Victoreen thimble was then compared with monitor thimbles located at suitable fixed positions outside the phantom. Two monitor thimbles were used so that irradiation would not be lost because of a faulty reading of a single monitor thimble. The average dose rate was the dose received by the sample divided by the time of irradiation. This value was, for a given experiment, either about 20 r or 40 r per minute. The betatron operates at 180 cycles per second, and the width of the roentgen-ray burst per cycle is of the order of 10 microseconds. Hence per second, the roentgen-ray output occurs in about 1/500 of the total time. The instantaneous dose rate is, therefore, about 500 times the average rate as calculated above.

High energy quanta above 1 mev. are absorbed primarily by pair production. The contributions due to scattering, photoelectric effect and Compton effect are insignificant. With 124 kv., on the other hand, the latter processes account for all of the absorption. It is true that the electrons in the 50 mev. machine are monoenergetic. However, when they strike a target, a so-called "Bremsstrahlung" spectrum of roentgen rays is produced. To a very rough first approximation this is an equal energy spectrum, that is the number of quanta in each energy range is such that each range carries the same energy. High energy quanta, however, produce pairs with a distribution in energy. The secondary roentgen rays produce other pairs, etc., as long as the roentgen-ray energy is above 1 mev. Just what the composition of the beam is at a given point in terms of energy distribution of electrons, positrons and roentgen-ray quanta is impossible to specify other than by the ionization in an instrument such as the Victoreen thimble chamber.

The distribution of dosage along the axis of the phantom as a function of depth was determined photographically and checked at appropriate points with thimble chambers. The two methods gave the same distribution within experimental error. The maximum of the depth dose in the phantom at 50 mev. is at approximately $3\frac{1}{4}$ inch depth in the phantom. Most of the irradiations of the wasps were made at this depth, but in a few cases it was done at two different depths simultaneously.

As Habrobracon adults are very small, about the size of Drosophila, they were enclosed in small gelatin capsules of size 0, which were inserted in a $\frac{1}{2}$ inch diameter hole drilled in a $\frac{1}{4}$ inch thick sheet of masonite, the center of the hole being in the beam axis. The sheet of masonite was then put at the proper depth in the phantom. The volume of the capsules was about the same as that of the thimble chamber.

Extensive discussions on the effect of a cavity in a medium, on the equilibrium of radiation and the medium in connection with dosage measurements have been published by Gray[5,6,7] and by Laurence.[14,15] It is believed that the dosage measurements in the irradiation of wasps fulfilled the necessary conditions. The volume of the cavity is small and is filled with air. Since the average atomic number of air and of the material of the phantom are both low and approximately the same, the cavity does not disturb the equilibrium between radiations and medium appreciably. In view of this the average body dosages as given by the Victoreen thimble chamber measurements are probably correct to ± 5 per cent.

It will be noted that the conditions under which the irradiations were carried out have been rather carefully stated. At and beyond the depth of maximum in the phantom ($3\frac{1}{4}$ inches) the primary quanta are in equilibrium with the secondary ionizing radiations. Since the Victoreen thimble is an ion chamber, it gives a measure of the ionization at the point

TABLE I

SUMMARY OF DATA ON HATCHABILITY OF FIRST MEIOTIC METAPHASE EGGS FOLLOWING TREATMENT WITH INCREASING DOSAGES OF 124 KV. AND 50 MEV. ROENTGEN RAYS

Dose	124 kv.					50 mev.				
	No. of experiments	No. of mothers	Eggs laid	Eggs hatched	Percentage of eggs hatched	No. of experiments	No. of mothers	Eggs laid	Eggs hatched	Percentage of eggs hatched
Control	3	57	1,735	1,606	92.6±0.6					
100 r	10	194	1,809	1,407	77.7±1.0	5	116	1,080	863	79.9±1.2
200 r	1	21	183	132	72.1±3.3					
250 r	9	159	1,417	922	65.1±1.3					
400 r	13	231	2,077	1,041	50.1±1.1	2	54	527	283	53.7±2.2
500 r	5	84	823	356	43.3±1.7	2	51	462	208	45.0±2.3
635 r						1	20	198	71	35.9±3.4
750 r	4	84	821	211	25.7±1.5	2	61	608	148	24.0±1.7
1,000 r	4	90	952	129	13.6±1.2	1	18	188	29	15.4±2.6
1,250 r	2	42	429	29	6.8±1.2					
1,500 r	15	297	2,648	156	5.9±0.5	3	75	722	73	10.1±1.1
1,750 r	6	112	1,102	64	5.8±0.7					

it is located, but it does not give a measure of the number of high energy quanta in the beam, since high energy quanta as such are not ionizing.

In comparative work of the kind reported in this paper, it is important that a cross-check be made of thimbles used in connection with the two machines, 124 kv. and 50 mev. Such a comparison of thimbles used at the General Electric Laboratory, at 1.5 mev., with the 100 r thimble chamber belonging to Union College appeared to indicate that the Union College owned 100 r thimble read about 3.5 per cent lower than the 100 r and 250 r thimble chambers at the Research Laboratory. This is small enough difference so that it seems to us that the experiments do compare the biological effects of equivalent amounts of ionization, read by Victoreen thimble chambers, and produced by the two different sources of roentgen rays.

III. RESULTS AND DISCUSSION

A summary of the data is given in Table 1. Inspection of this will show that the control hatchability is high (92.6±0.6 per cent). Comparison between hatchability percentages for 124 kv. and 50 mev. and for corresponding dosages in the range extending from 100 r to 1,000 r indicate no statistically significant differences between the two types of radiation; but comparison of the two percentages at 1,500 r reveals an ostensibly real difference. For given dosages the differences are small, but for all dosages except one (750 r) such deviations are in a direction which might suggest that the 50 mev. radiations are less effective. Since the results seem to approximate simple exponential functions, one way of examining for differences between the two types of radiation is to calculate the two lines which best fit the data and then to test for difference in slopes. The plots of the logarithms of the per cent survival of eggs against dose are given in Figure 1. The equations, when unweighted data are used, are as follows:

$$124 \text{ kv.} \quad y = 1.987586 - 0.000787\ r$$
$$50 \text{ mev.} \quad y = 1.966127 - 0.000685\ r$$

Use of weighted data makes very little difference in the slopes, 0.000778 and 0.000658 for 124 kv. and 50 mev., respectively.

The question as to whether there is a significant difference between the slopes, when unweighted data are used, can be answered by the following variance analysis.

Deviations from Individual Slopes		*Differences among Slopes*	
d/f	M.S.	d/f	M.S.
15	0.0057	1	0.0116

The above calculations give an F value of 2.03 which, for these degrees of freedom, indicates no significant difference. The F

value would have to be as large as 4.54 for a 0.05 level of significance. Ordinarily the results for 1,500 r would suggest further work at higher dosages. This is quite evidently impossible with these eggs since even at 1,500 r the work is done rather close to the completely lethal dose.

Further analysis was directed toward answering the question of whether the data are uniform among experiments under the same treatment. Inspection of Table II, which gives the analysis of variance within dose, shows that although some significant differences are indicated, most of the comparisons are not significant. The analysis as a whole seems to show that the experiments conveyed the same information even though they were done at different times. Most of the starred values occur in comparisons of mean squares among females with mean square within females. Biologically this might indicate that the eggs of different females were differentially susceptible to roentgen rays. However, in most cases the degrees of freedom are fairly large. When this is the case, significance may be indicated even though the biological difference is so small as to be of little practical importance. The analysis for controls indicates that there may have been some difference in hatchability depending upon whether the eggs were stored or laid continuously. However, the difference between 93.9 per cent for those laid continuously and 90.5 per cent for stored eggs is neither very large nor significant. Control data were therefore combined.

The analysis within dose answers some questions, but these are only indirectly related to the main problem of comparing the effects of high and low voltage radiations. Further interpretation raises the question of whether the data for a given dose can be regarded as though they were conveying the same information regardless of whether the radiations were delivered by the 124 kv. machine or the betatron. An analysis directed toward answering this question is given in Table III. Again, most of the comparisons indicate no significant

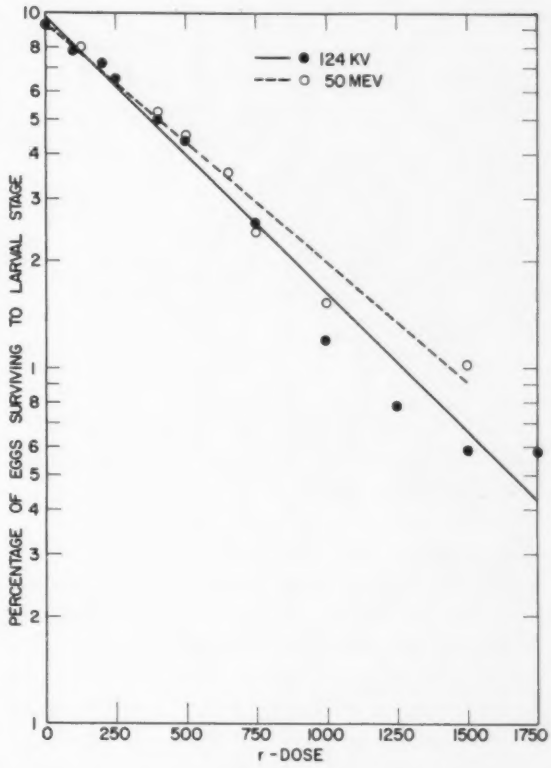

FIG. 1. Survival to larval stage of unfertilized eggs treated in first meiotic metaphase. Lines were fitted by method of least squares.

differences. It appears that one kind of radiation could be substituted for the other. If this conclusion is considered together with the deduction previously drawn, that there is no difference in the slopes of the fitted lines, it seems to follow that under the conditions of these experiments, roentgen rays from the 50 mev. machine and those from the 124 kv. machine are equivalent in effect.

The above conclusion is in agreement with that drawn from the work of Clark and Sykowski on lens cataract and of Fritz-Niggli on Drosophila embryos, but it differs from that drawn from the work of others on sex-linked recessive lethals in Drosophila, hair decoloration of mice, yeast, clinical experience with the human, as previously cited. It is not clear whether the difference in results is attributable to variations in technical methods involved in the use of machines, to differences inherent

Table II

ANALYSIS OF VARIANCE WITHIN DOSE

	Controls				124 kv.															
	Eggs laid continuously		Eggs stored		100 r		200 r		250 r		400 r		500 r		750 r		1,000 r		1,250 r		1,500 r		1,750 r	
	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.
Among experiments	1	.0202†	10	.0957	9	.1642			8	.3191	12	.2223	4	.1141	3	.3409	3	.1532	1	.0783	14	.1499†	15	.0831
Among females within experiments	67	.2105†	89	.0628	184	.2137*	20	.3267*	150	.3204†	218	.3140*	79	.2840	80	.1928	86	.1249	40	.0521	282	.0589	106	.0704*
Within females among eggs	604	.0725	962	.0566	1,615	.1683	162	.1867	1,258	.2158	1,846	.2428	739	.2423	737	.2127	862	.1164	387	.0643	2,351	.0545	990	.0529
Total	672		1,061		1,808		182		1,416		2,706		822		820		951		428		2,647		1,101	

	50 mev.													
	100 r		400 r		500 r		635 r		750 r		1,000 r		1,500 r	
	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.
Among experiments	4	.3298	1	.0404	1	.2250			1	.0942			2	.3379
Among females within experiments	111	.2271†	52	.3110	49	.2651	19	.2481	59	.2801†	17	.1672	72	.1237†
Within females among eggs	964	.1524	473	.2428	411	.2461	178	.2294	547	.1724	170	.1275	647	.0866
Total	1,079		526		461		197		607		187		721	

* Level of significance is between .05 and .01.
† Level of significance is less than .01.

TABLE III

COMPARISONS BETWEEN 124 KV. AND 50 MEV.

	100 r		400 r		500 r		750 r		1,000 r		1,500 r	
	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M.S.
Between 124 kv. and 50 mev. experiments	1	.3061	1	.5388	1	.0921	1	.0995	1	.0552	1	1.0100
Among experiments	13	.2152	13	.2083	5	.1363	4	.2792	3	.1532	16	.1734
Among females within experiments	295	.2189*	270	.3133*	128	.2768	139	.2299	103	.1319	354	.0721
Within females among eggs	2,579	.1624	2,319	.2428	1,150	.2437	1,284	.1827	1,032	.1182	2,898	.0635

* Level of significance is less than .01.

in the biological materials used for testing or perhaps to a combination of these. A rather detailed description of the use of machines and methods of dosimetry used in these experiments has already been given. A discussion of the biological material from the point of view of how low voltage roentgen rays lead to death of Habrobracon eggs is, then, of considerable importance.

Studies of the cytology and development of the eggs following irradiation are to be found in the works of Whiting.[21,22] These show that eggs, after being laid, form polar bodies, cleave and sometimes develop up to blastoderm. Chromosomal fragments (largely terminal deletions) were found at all stages from first meiotic metaphase through various stages of cleavage. Chromosome bridges were seen not in first meiotic anaphase, but at almost any anaphase stage thereafter, including second meiotic anaphase. Percentage of eggs with one or more detectable deletions was highly correlated with percentage of eggs which died following treatment with various dosages. Such a picture indicates that embryos die at a stage when chromosome balance becomes so disturbed that cells cannot function. Most eggs die, therefore, because they are bearers of one or more dominant lethals. Later work (Heidenthal, 1952) has shown that following roentgen irradiation a small percentage of the eggs bear recessive lethals. Genetic and cytological evidence, then, indicates that haploid eggs treated in first meiotic metaphase die because dominant lethals and to a much lesser extent recessive lethals have been induced in one or more of the chromosomes.

A second line of indirect evidence supports the idea that the lethal effect at the doses used is in the nucleus, not the cytoplasm. In this connection, Whiting[23,24,25] has reported that androgenetic males sometimes develop from eggs heavily irradiated in first meiotic metaphase if these are later fertilized by normal sperm. These male progeny are in a sense motherless because the female pronucleus does not take part in the development which leads to their production. Cytological observations show that in a small percentage of heavily irradiated metaphase eggs chromosome bridges restrain the movement of the egg pronucleus from migrating to the usual position where fusion of egg and sperm pronuclei normally occurs. Under these conditions the egg pronucleus fails to function. Androgenetic work was done at very high dosages —up to 54,075 r. The frequency of androgenetic males was low at any dose, but highest at about 15,000 r. These observations make it seem most unlikely that eggs treated with dosages of 500–1,500 r die because of lethal injury to the cytoplasm, since androgenetic males develop from a normal nucleus supplied by the father, surrounded by very heavily irradiated cytoplasm contributed by the mother. Androgenetic males appear to be normal in all respects, but show inheritance of a trait like eye color only from the father. Their low frequency is explained by the fact that

Table II

ANALYSIS OF VARIANCE WITHIN DOSE

	Controls				124 kv.															
	Eggs laid continuously		Eggs stored		100 r		200 r		250 r		400 r		500 r		750 r		1,000 r		1,250 r		1,500 r		1,750 r	
	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.
Among experiments	1	.0202†	10	.0957	9	.1642			8	.3191	12	.2223	4	.1141	3	.3409	3	.1532	1	.0783	14	.1499†	15	.0831
Among females within experiments	67	.2105†	89	.0628	184	.2137*	20	.3267*	150	.3204†	218	.3140*	79	.2840	80	.1928	86	.1249	40	.0521	282	.0589	106	.0704*
Within females among eggs	604	.0725	962	.0566	1,615	.1683	162	.1867	1,258	.2158	1,846	.2428	739	.2423	737	.2127	862	.1164	387	.0643	2,351	.0545	990	.0529
Total	672		1,061		1,808		182		1,416		2,706		822		820		951		428		2,647		1,101	

	50 mev.													
	100 r		400 r		500 r		635 r		750 r		1,000 r		1,500 r	
	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.
Among experiments	4	.3298	1	.0404	1	.2250			1	.0942			2	.3379
Among females within experiments	111	.2271†	52	.3110	49	.2651	19	.2481	59	.2801†	17	.1672	72	.1237†
Within females among eggs	964	.1524	473	.2428	411	.2461	178	.2294	547	.1724	170	.1275	647	.0866
Total	1,079		526		461		197		607		187		721	

* Level of significance is between .05 and .01.
† Level of significance is less than .01.

Table III

COMPARISONS BETWEEN 124 KV. AND 50 MEV.

	100 r		400 r		500 r		750 r		1,000 r		1,500 r	
	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M. S.	d/f	M.S.
Between 124 kv. and 50 mev. experiments	1	.3061	1	.5388	1	.0921	1	.0995	1	.0552	1	1.0100
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bridges formed between egg pronucleus and polar body are usually not restraining. As a rule, the egg pronucleus bearing dominant lethals reaches the normal position where egg and sperm pronuclei unite in spite of the presence of bridges. Dominant lethals then kill the zygote.

The observations and reasoning just cited lead to the conclusion that embryos failed to hatch as larvae primarily because ionizing radiation induced chromosome breakage; that this in turn led to severe disturbance in chromosomal balance; that failure of embryos to hatch was attributable to the presence of dominant lethals. Whiting's analysis accounts only for death of Habrobracon eggs. The same mechanisms may or may not play a decisive part in lethal damage to other cells and in other organisms. It seems plausible, too, to think that perhaps the equivalence in effectiveness of the high and low voltage radiations may hold for some mechanisms and conditions of irradiation, but not for others. The problem of equivalence is obviously complex.

IV. SUMMARY

First meiotic metaphase eggs of Habrobracon were used to test the comparative effectiveness of 124 kv. and 50 mev. roentgen irradiations. Dosages ranged from 100 r to 1,750 r for low voltage, and from 100 r to 1,500 r for high voltage studies. Failure of unfertilized eggs to hatch has been attributed to the presence of dominant and, to a lesser extent, of recessive lethals. Dose action curves are approximately exponential. Test for difference between the slopes of the two curves when these were plotted and fitted on a semi-logarithmic scale revealed no statistically significant difference. Variance analysis of data within dose and for each voltage of radiation used showed that the data for each dosage appeared to be conveying the same information from experiment to experiment. Comparisons between 124 kv. and 50 mev. data indicated that for a given dosage radiations of low and high voltage were revealing similar effects.

A review of previous work by Whiting, on which the method was based, has led to the conclusion that roentgen irradiation has induced chromosome breakage, terminal deletions and the formation of chromosomal bridges in most of the eggs which died. Thus dominant lethals were mainly responsible for failure of eggs to hatch as larvae.

V. CONCLUSION

Equivalent roentgen-ray dosages from 124 kv. and 50 mev. machines appear to be equally effective in inducing lethals in Habrobracon eggs treated in the first meiotic metaphase.

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THE EFFECT OF GAMMA RADIATION ON THE CENTRAL NERVOUS SYSTEM*†

II. THE EFFECTS OF LOCALIZED IRRADIATION FROM TANTALUM 182 IMPLANTS

By EDGAR A. BERING, JR., ORVILLE T. BAILEY, FRED D. FOWLER, PETER H. DILLARD, *and* FRANC D. INGRAHAM

RADIOACTIVE tantalum (Ta^{182}) has been used to study the effects of gamma radiation administered locally to the central nervous system. This paper, which is the second report of this problem,[5] describes the method, including dosimetry, and observations in a series of acute experiments. The late histological changes will be reported separately.

The early investigations of the reaction of the central nervous system to irradiation were limited by primitive roentgen-ray equipment and by a paucity of radioactive substances. The first work done on experimental techniques for irradiating the nervous system was published by Tarkhanov[86] in 1896. He noted that the reflexes were slowed in frogs and that flies became sluggish after exposure to roentgen radiation. Other investigations during this early period employed unshielded rays of uncertain dosage and in the animals used, frogs,[86] guinea pigs,[36,43,61,71] rabbits,[42,71,75] turtle doves[43] and mice,[36,75] the principal changes noted consisted largely of varying degrees of lethargy and paralysis.

Danysz[21,22] in 1903 was the first to use radium for experimental irradiation. He found that its application to the skin of mice would result in superficial necrosis, and its insertion under the scalp in convulsions and death. He also irradiated animals by fastening 50 mg. of radium to the top of their cage, thereby producing paraplegia. For all of these experiments, large quantities of unfiltered radium were used and the main pathological finding was hemorrhage into the tissues of the central nervous system. This work was repeated essentially by other investigators[2,45,46,80] with similar results.

In 1911 Horsley and Finzi[37] used a filtered radium source directly on the brain. They applied 55 mg. for two and one-half and four hours to the motor cortex of monkeys and stimulated the area electrically before and after irradiation. In their experiments they found that stimulation after irradiation failed to produce movements. The animals were sacrificed in twenty-six to forty-five days and the pathological findings consisted of leptomeningeal thickening, endothelial proliferation in the blood vessels, and punctiform hemorrhages into the cerebral substance. No changes were noted in the nerve cells or neuroglia.

Between 1910 and 1920 better methods of roentgen-ray filtration and dosage standardization were developed, and the work done during this period[6,8,11,13,88] was more carefully controlled in these respects. However, these studies were usually confined to one or two selected doses and because of the different units of measurement employed, as well as other uncontrolled factors, the exact relationship between tissue exposure and pathological findings cannot be accurately determined by comparing them. In none of these investigations were the important delayed effects of radiation examined.

In 1920, Bagg[3,4] first used radon seeds under the scalp and compared the effects

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of a filtered source with those of an unfiltered one. He found that the unfiltered radiations would produce rapid onset of neurologic disturbances with hemorrhage into the brain and thrombosis of the blood vessels. The filtered source produced much less damage. When it was applied to the scalp of dogs in "9000 mc. hr." dose there was only epilation and no neurologic disturbance or alteration in the gross appearance of the brain. Edwards and Bagg[26] later used radon seeds in the corpus striatum to produce a progressive destructive lesion as a means of studying the physiologic dysfunction thus produced.

The first series of acute experiments making use of graded doses of radiation from a well filtered source was carried out in 1920 by Williamson, Brown and Butler.[93] They used a 2.5 cm. capsule containing 50 mg. of radium shielded by 0.4 mm. of platinum and applied it to the motor cortex of dogs for four to eighteen hours. One animal out of the 7 in their series showed convulsive movements. On the basis of their pathological findings of necrosis and hemorrhage they felt that this source had a destructive effect for 5 mm. after an exposure of 900 milligram hours. A similar technique was used by Pendergrass *et al.*[62] in 1922 who found that 1,000 mg. hr. of exposure to radium (0.4 mm. Pt filter) produced diffuse cerebral swelling. Therefore, they advised against the use of radiation in spinal tumors and considered its use in cerebral neoplasm only if the growth was easily accessible and if the skin could be well protected.

The production of paraplegia in cats by varying doses of radon implanted next to the spinal cord was investigated by Cairns and Fulton[15] in 1930. They found that shielded doses of less than 4 mc. produced no neurologic changes, but that those of more than 9.5 mc. would produce eventual total paralysis.

Several studies have been done on the influence of radiation on the production of cerebrospinal fluid. In 1924, Marburg[49] stated that roentgen irradiation would relieve headache due to increased intracranial pressure by temporarily suppressing the production of cerebrospinal fluid. Inaba *et al.*,[38] in 1927, established curves for the rate of cerebrospinal fluid drainage from a cannula in the cisterna magna of dogs. After an 80 per cent erythema dose of roentgen radiation, the rate of drainage was decreased, especially in the period between ten and fourteen days after irradiation. On histologic examination they found that the nuclei in the cells of the choroid plexus were slightly pyknotic. However, Heidrich *et al.*,[35] in 1929, were unable to find a change in fluid production after irradiation. Skefer[83] states that small doses of roentgen rays diminish the production of cerebrospinal fluid, whereas large doses at first stimulate and then later depress it.

Nemenow[58] in 1934 attempted to evaluate the physiologic alterations in the nervous system due to irradiation by observing the changes produced in conditioned reflexes in dogs. He found that doses of 1,500 roentgens and over would produce a state of inhibition in the conditioned reflexes. He considered this a more delicate criterion of dysfunction than the usual clinical and pathological techniques.

In 1937, Colwell and Gladstone[19] were the first to study the delayed effects of irradiation. They applied a standard dose of radium (14.6 mg.) to the scalp of rats for three hours and then allowed the animals to recover. Examinations were carried out after varying lengths of time and they found an inflammatory reaction which increased with the length of time since irradiation.

Some detailed pathological examinations were carried out in the past,[24,25,26] but in general there was not good enough control of the experimental method to allow a valid comparison of results. Recently, however, carefully regulated single doses of filtered roentgen rays have been administered to rhesus monkeys,[23] dogs[53] and rabbits[72] and the animals kept until symptoms developed or death intervened. In 1949, Russell[72]

made a careful pathological evaluation of some of this material and has concluded that while there may be an early diffuse neuronal response, the main factor in producing late damage in the central nervous system is a progressive vascular reaction.

Borison and Wang[12] used small doses of radon in gold and glass seeds to determine the size of a lesion produced by a given amount of radiation. The two types of seeds allowed them to gather data on both beta and gamma radiation. They found the area of demyelinization to be a direct function of the total dose received, and with glass seeds the size of the lesions could be predicted with fair accuracy. Their histological studies were limited by lack of special stains but within their stated limits they give a description of the acute effects of irradiation.

Hicks[39] has recently reported a study of the effects of irradiation on the developing embryo. His studies show that relatively small doses of radiation will produce profound effects on the developing nervous system. These changes apparently result from the destruction of neuroblasts and the form of the malformation is dependent upon the moment in gestation when the irradiation takes place.

Schaeffer and Jacob,[73] in 1925, were the first to call attention to the dangers of irradiating intracranial lesions in clinical practice. In 1926, Béclère[9,10] classified the types of untoward effects that might result from intense radiation therapy. He made special mention of the occurrence of acute cerebral edema (prereaction) when large doses of radiation were given in a short period of time or without sufficient filtration. To avoid skin flap necrosis and injury to normal tissues, Elsberg, Davidoff and Dyke[29] recommended that the irradiation of tumors be carried out through the open wound at operation.

Over the past twenty years many case reports of brain damage due to irradiation have appeared in the literature.[30,47,52,63,64,79,84,87] Associated with our increasing cognizance of this danger has been an increase in interest in the changes produced in the normal human brain by irradiation.[1,59,91,92] However, in human material the dose received in normal tissue is not usually calculated apart from the estimated tumor dose. In many instances, the filtration factors and duration of therapy are not constant, and thus it is not easy to reach any general conclusions from these individual case reports.

Warren,[91] in 1943, in a general review of the effects of radiation on the nervous system concluded that peripheral nerves and the autonomic system were highly resistant to radiation.

The availability and use of radioisotopes for medical, industrial and military purposes has created a need for precise knowledge of the isolated biological effects of radiation. Only with this knowledge can the isotopes be used most effectively with the greatest safety. Any attempt to generalize the accumulated data is frustrated by the diffuse changes recorded and the problems of dosimetry. There is, however, some general agreement which will be brought out in the discussion of the results of these experiments.

The effect of any lesion on the central nervous system is a function of the site of the lesion and, therefore, when the physiological and histopathological responses to radiation are completely understood, then clinical effects can be predicted. These responses must be studied not only in the acute phase, but through the late stages as well.

MATERIALS AND METHODS

Radiation Source. The tantalum (tantalum 182) used as a radiation source was produced by irradiating tantalum 181 wires in an atomic pile. Ta^{182} has a half-life of 117 days emitting both beta and gamma radiation. The beta radiation has a maximum energy of 0.53 mev. and the gamma energies in mev. are 1.22 (57 per cent), 1.13 (37 per cent), 0.22 (4 per cent), and 0.15 (2 per cent) with internal conversion noted in the low energies.[64] Two sizes of wire were used;

they measured 1 by 5 mm. and 1 by 10 mm. Each piece was assayed with a Lauritsen electroscope and encased in a polyethylene tube for ease of handling. Both polyethylene[39] and tantalum[5,14] have been shown to be relatively inert in cerebral tissue.

Animals and Irradiation Technique. Eighteen monkeys were used for this series of experiments; 12 were *Macaca mulatta* and 6 were *Ateles geoffroyi*. The external morphology of the brains of the two genera are sufficiently similar for the purposes of these experiments. A point 1.5–2.0 mm. posterior to the motor strip was selected as the irradiation site. This allowed maximum irradiation with minimum neurological deficit. The Ta^{182} wires were implanted approximately 1.5 mm. into the brain through small drill holes which were made under nembutal anesthesia. When the calculated amount of radiation had been delivered, the animals were sacrificed and the wires removed. Complete autopsies were carried out immediately. A typical protocol is given in detail.

Typical Animal Protocol.

June 22, 1951: Implantation of radioactive tantalum 182.

Tantalum 182 piece No. 2
Time of implant—1240
Original activity—3.5 mc.
Time to be left in brain—18 d., 4½ hr.
Total dose received at 3.0 cm.—900 r.

Anesthesia 1.2 cc. intravenous nembutal. A small incision was made over the right parietal boss 3.0 cm. from the occipital protuberance and 1.5 cm. from the midline. A drill hole was made in the skull and the dura exposed. The dura and pia were then perforated with a No. 16 needle. Sutures were placed in the subcuticular layer ready for tying immediately after the implantation. Piece No. 2 of Ta^{182} was inserted through the perforated dura and into the substance of the brain for a distance of 1.5 cm. The previously placed sutures were then tied and the animal returned to its cage in good condition.

June 25, 1951: Wound healing well; animal active with no evidence of weakness.

July 6, 1951: No evidence of hemiparesis. There is beginning to be some dryness and scaling of the scalp over the implantation site.

July 10, 1951: At the time of sacrifice the animal still showed no motor weakness and no sensory loss could be detected. There was a scar over the implantation site and increased dryness of the surrounding skin. The scalp was removed over the implantation site and placed in Bouin's fixative. The Ta^{182} was then removed and the bone removed from about the implantation site and placed in fixative also. The dura showed some opacity near the source of irradiation but otherwise was normal. The central nervous system was removed intact with dura and placed in 10 per cent formalin saline. Specimens of heart, lung, liver, spleen, kidney, mesenteric lymph node, pancreas, and femoral bone marrow were placed in fixative.

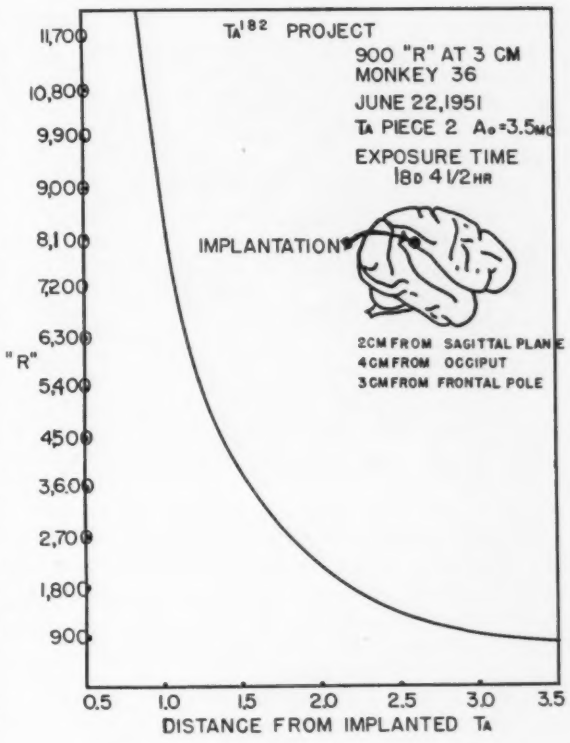

FIG. 1. Irradiation data sheet kept for each animal.

Dosimetry. (For irradiation data see Fig. 1.) All doses are expressed in roentgens delivered to the tissue. Sufficient data are given so that they can easily be converted into other units if it becomes desirable. The beta rays from Ta^{182} have a soft tissue range of only about 1.2 mm. and the polyethylene sheath reduces this value even more. Thus the tissue dose received beyond 3 mm. may be computed on the basis of gamma-ray energy alone. On the basis of data given by Marinelli, Quimby and Hine,[80] the gamma energy of Ta^{182} is found to produce 6.124 roentgens per millicurie hour at 1.0 cm. in air (Table 1). By applying the soft tissue linear absorption coefficient of 0.03 (80), Ta^{182} is found to produce 5.94 roentgens per hour in soft tissue at 1.0 cm. from a 1.0 mc. source, or 14.9 roentgens per day at 3 cm. from a 1 mc. source.

TABLE I

TOTAL GAMMA-RAY DOSE DELIVERED BY TANTALUM 182 AT 1 CM. IN AIR

Gamma-Ray Energy mev.	(50) r/mc. hr. at 1.0 cm. in Air	(66) Relative Intensity	Contribution to Total Dose in Roentgens
1.22	6.6	0.57	3.762
1.13	6.22	0.37	2.301
0.22	1.2	0.04	.048
0.15	0.67	0.02	.013
Gamma-ray dose in r/mc. hr. at 1.0 cm. in air			=6.124

Because of the moderately long half-life of Ta^{182}, the radioactive decay which occurs during the administration of small doses of radiation is not significant. For longer intervals, however, this must be taken into consideration. A general formula for calculating the total dose given may be obtained by integrating the radioactive decay curve with respect to time.

Thus:

I. $A = A_0 e^{-\lambda t}$
where A_0 = initial activity of source in millicuries.
A = activity at any time t
λ = decay constant
t = time in days
Integrating I with respect to time.

$$\text{Millicurie days} = \frac{A_0(1 - e^{-\lambda t})}{\lambda}$$

for Ta^{182}, $\lambda = 0.005924$

II. Millicurie days = $169\ A_0\ (1\text{-}e^{\text{-}.005924t})$
1 mc. Ta^{182} delivers 14.9 roentgens per day at 3 cm. in soft tissue.

III. Roentgens at 3.0 cm. from source in tissue = $2518\ A_0\ (1\text{-}e^{\text{-}.005924t})$
If the source is left in the tissue permanently t = infinity

IV. Total available dose as roentgens delivered in tissue at 3.0 cm. from source = $2518\ A_0$

For convenience in calculating the tissue dose at varying distances from the implant, a graph which includes tissue absorption as well as attenuation by distance was made for each animal (Fig. 1). The calculations for these charts were made on the basis of a point source of irradiation. The error introduced by this assumption varies in relation to the length of the wire and the distance from it.[44] With a 5 mm. wire the error at 1.0 cm. is only 2 per cent and decreases as the distance increases. This is well within the error of interpretation of these experiments.

No estimations of energy absorbed were made because the delivered dose varied so rapidly in the tissue under consideration that accurate calculations become excessively cumbersome.

RESULTS

Out of 18 animals irradiated, 4 were considered to be unsuitable for use; 3 of these died shortly after operation from pneumonia or tuberculosis, and 1 had gross inflammation about the wound. It must be remembered when considering these results that they are acute experiments, and if the animals had been allowed to survive the results would have undoubtedly been altered with time.

Clinical Effects. No animal in this group died as a result of the radiation received. This is probably a reflection of the location and relatively small volume of tissue which was actually irradiated.

Gross neurological deficit did not appear until a dose of about 2,250 r at 3 cm. had been given. Animals receiving this amount of radiation developed a mild hemiparesis; with larger doses of radiation the hemiparesis was more pronounced. In all animals the weakness was gradual in its onset and was related to the radiation received rather than traumatic effects of the implantation.

Skin and Scalp. None of the animals regrew hair directly over the implantation site. This was partially due to the early sacrifice dates of some animals, but where the survival was over ten days, the effect must be attributed to the irradiation. With the highest doses the area epilation was about 5 cm. in diameter. This indicates that about 2,000 r will cause epilation in the monkey when delivered at the rate and energy of these experiments.

As the skin dose approached 3,800 r, dryness and scaling were noted; around 5,800 r, the subcutaneous tissues were thick and immobile. At approximately 9,500 r, there was degeneration of the surface layer, leaving a raw, moist, nonhealing area. The highest doses given (about 20,000 r) caused

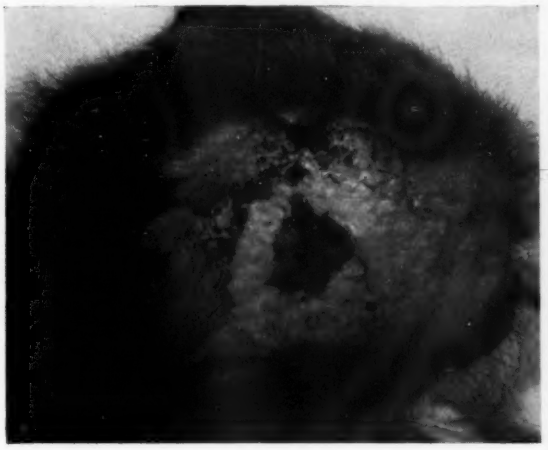

Fig. 2. M-1-51. Maximal area of necrosis produced by 6,612 r at 2.0 cm. given over a period of 72 days.

necrosis of skin and scalp over an area of about 1.5 cm. in diameter, centered over the implantation site (Fig. 2).

Bone. The low doses caused no visible gross changes in the bone, but with the highest doses the bone overlying the implant became necrotic and spongy in appearance.

Meninges. The dura mater was unchanged with small doses of radiation, but above 430 r at 3 cm. it seemed to become white and opaque over an increasingly large area. However, even with maximum doses of 4,800 r at 3.0 cm. from the source,

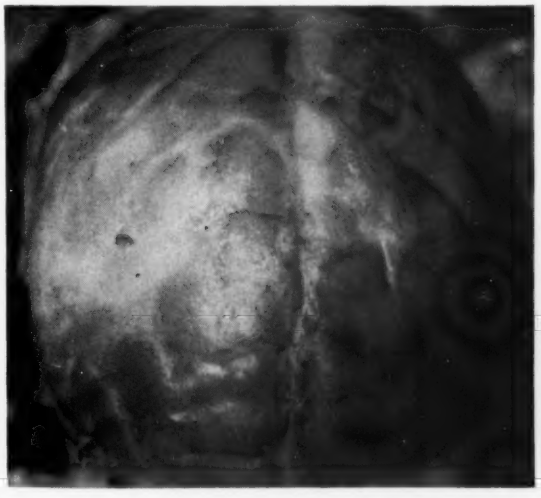

Fig. 3. M-1-51. Opacity of the dura mater over the right hemisphere; 6,612 r at 2.0 cm. given over a 72 day period.

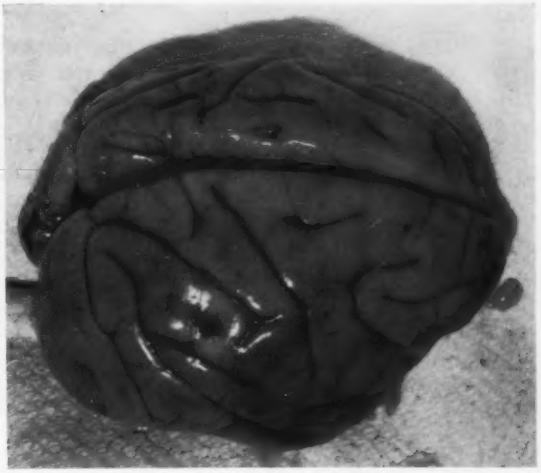

Fig. 4. M-36-51. Early pallor about the implantation site; 8,000 r at 1.0 cm. given over 18 day period.

this did not extend beyond 2.5 cm. from the implant (dose at this point was about 6,700 r) (Fig. 3).

There was no observable gross alteration in the leptomeninges, but the pial and cortical vessels were slightly engorged around the irradiated areas at doses greater than 2,000 r at 3 cm.

Brain. Concomitant with changes in the dura were alterations in the brain itself. There was slight pallor seen in the brains where the dose was 430 r at 3.0 cm., and with 2,250 r at 3 cm. there was an area of frank necrosis extending out from the implant for a distance of about 0.75 cm. (Fig.

Fig. 5. M-35-51. Frank necrosis of the brain after 21,500 r at 1.0 cm. given over 47 day period.

TABLE II

A SUMMARY OF THE ACUTE GROSS EFFECTS OF GAMMA RADIATION FROM A TANTALUM 182 SOURCE IMPLANTED IN THE BRAIN

Monkey	Initial Activity of Source	Exposure Time	Calculated Dose Delivered at			Gross Observations at Time of Sacrifice			
			1 cm. r	2 cm. r	3 cm. r	Clinical neurological changes	Skin and scalp (about 1.5 to 2 cm. from source)	Dura mater	Brain
12	2.5 mc.	1.3 hr.	23	3.3	2.4	None	None	None	None
7	2.85 mc.	2.25 hr.	40	5.8	4.2	None	None	None	None
9	2.85 mc.	5.5 hr.	96	14	10	None	None	None	None
20	2.68 mc.	13 hr.	182	58	19	None	None	None	None
8	2.85 mc.	18.1 hr.	315	45	33	None	None	None	None
15	2.75 mc.	2.1 days	823	119	86	None	None	None	None
13	2.80 mc.	4 days	1,720	248	180	None	None	None	None
21	2.64 mc.	11.2 days	4,100	591	430	None	Epilation	None	Slight blanching of brain around implant
36	3.5 mc.	18.2 days	8,600	1,206	900	None	Epilation with dryness and scaling of scalp over implant	Slight opacity and thickening around implant	Pallor of brain around implant
17	5.0 mc.	13.3 days	9,556	1,377	1,000	None	Epilation fluid, and gelatinous matter beneath scalp	Slight thickening and opacity near implant	Brain white around implant. Remainder of hemisphere diffuse inflammation
32	4.35 mc.	22 days	12,900	1,858	1,350	None	Epilation 2.5 cm. diam. 1 cm. diam. area on scalp thick and immobile	Thick and opaque area 2 cm. in diam.	2 cm. around implant site blanched and white
35	3.75 mc.	47 days	21,500	3,097	2,250	Minimal left hemiparesis	Scalp desquamated and raw	Thick and opaque over implant site	Area of necrosis around implant site 1.5 cm. in diameter
10	5.45 mc.	55 days	36,300	5,229	3,800	Left hemiparesis +++	Scalp epilated and desquamated	Thickened	Wide area of blanching around implant. Remainder of brain hyperemic
1	5.64 cm.	72 days	45,900	6,612	4,800	Left hemiparesis ++++	Epilation 5 cm. diam. Area of necrosis 1.5 cm. in diam.	Area thickened and opaque 2.5 cm.	Brain generally suffused with necrosis about implant site

3). (The dose received at the perimeter of the necrotic area was approximately 36,000 roentgens.) As the dose at 3 cm. was increased, the brain tended to be hyperemic, and in one animal the irradiated hemisphere had turned very light reddish brown color (Fig. 4 and 5).

Other Organs. No gross alterations which could be attributed to the irradiation were present in the other organs examined.

The results are summarized in Table II.

PATHOLOGICAL FINDINGS

The histopathological effects in the skin of the scalp in these animals were similar in all details to those produced by roentgen irradiation. They were, however, of peculiar severity and were present in all monkeys from which tissue was examined, even when the skin grossly showed little or no detectable change.

The brains, after fixation in 10 per cent formalin, were sectioned in coronal planes.

Table III

A COMPARISON OF REPORTED EFFECTS OF IRRADIATING THE CENTRAL NERVOUS SYSTEM. DOSES GIVEN IN ROENTGENS DELIVERED ARE APPROXIMATE CALCULATIONS BASED ON DATA TAKEN FROM REPORTED EXPERIMENTS

Author	Animal	Source of Radiation	Site Irradiated	Total Dose	Irradiation Time	Clinical Neurological Effects
Davidoff et al.[23]	Monkey	X-ray (200 kv.)	Spinal cord	1,000 r	17 min.	No clinical effect
				4,000 r	69 min.	Paraplegic for 1 year then died
				5,000 r	85 min.	Paraplegic and death in 3 days
			Cerebrum (open wound)	2,000–3,000 r	51 min.	Threshold for neurological signs. Hemiparesis after several months
				4,000 r	68 min.	Contralateral hemiparesis within 24 hr.
				4,800 r	82 min.	Died in 7 days
				7,200 r	123 min.	Died in 5 days
			Cerebellum	3,000 r	51 min.	No signs for 6 mo.
				4,000 r	68 min.	Ataxia after 5 mo.
				5,000 r	85 min.	Ataxia in 3½ mo. Died in 4 mo.
Carty and Ray	Dog	X-ray (60 kv.)	Skull and dura	12,000 r or less	120 min.	6 animals showed no gross changes up to 5 mo.
				18,000 r	180 min.	Immediate lethargy and vomiting contralateral hemiparesis in 7–10 days
Russell et al.[72]	Rabbits	X-ray (200 kv.)	Skull, external	2,030 r	13 min.	No clinical abnormality in 25 mo.
				2,440 r	16 min.	Neurologic signs at 240 days
				2,850 r	18 min.	After 100 days became irritable, anorexic and developed neurological signs
Hicks[39, 40]	Pregnant Rats, Mice	X-ray (200 kv.)	Total body irradiated	35–600 r in 8 steps		200–400 r produced severe destruction of rapidly growing regions of the brain. 150 r destruction to less degree. There were other lesions and maldevelopments
Horsley and Finzi[37]	Monkey	Radium	Brain	500 r at 1 cm.	2.5 hr.	No clinical neurological changes
				1,250 r at 1 cm.	4 hr.	No neurological changes
Williamson et al.[93]	Dogs	Radium		1,164 r to 7,200 r at 1 cm.	4 hr. 12 hr.	One animal of 7 had a seizure
Pendergrass et al.[62]	Dogs	Radium	On surface of brain	1,944 r at 1 cm.	3 hr.	No clinical changes observed in 11 mo.
				6,210 r at 1 cm.	10 hr.	This dose was threshold for clinical effects from a well filtered source
				7,560 r at 1 cm.	12 hr.	With this dose and above, all animals died
			Spinal cord (dose calculated at center of cord)	5,400 r	3 hr.	No clinical effect
				10,800 r	6 hr.	Paraplegia in 7 weeks
				16,200 r	9 hr.	Paraplegia in 3 weeks
				21,600 r	12 hr.	Paraplegia in less than 2 weeks
Ross[70]	Rabbits	Radium	Intracortical implant	600 r at 1 cm.	3–24 hr.	Local necrosis with hemorrhage and death
Colwell and Gladstone[19]	Rat	Radium	External to scalp	289 r at 1 cm.	3 hr.	Killed at varying lengths of time. Increasing inflammation noted as time following exposure increased

TABLE III (Continued)

Author	Animal	Source of Radiation	Site Irradiated	Total Dose	Irradiation Time	Clinical Neurological Effects
Cairns and Fulton[15] (These calculations assume the published dose is the strength of the radon seeds used)	Cats	Radon	Spinal cord, intradural (dose calculated for center of cord)	31,920 r	Total	This dose or less caused no clinical effect
				5,298 r	1st day	
				50,220 r	Total	This dose and greater caused paraparesis in 8 days or less
				8,336 r	1st day	
				75,810 r	Total	This dose and greater caused complete paraplegia in 5 days or less
				12,584 r	1st day	
				48,420 r	30 hr.	Showed weakness at this time
	Monkeys			71,820 r	Total	This dose and less showed no effect
				11,922 r	1st day	
				94,140 r	Total	Slight paraparesis beginning after three days
				15,627 r	1st day	
Campbell and Novick[16]	Cat	Radon	Surface of cortex	Approx. max. 3,300 r		No gross clinical effects Lysis of astrocytes in superficial layers
Borison and Wang[12]	Dog	Radon	Intramedullary	678 r at 1 cm. in air	Total	This dose or more given ½ in each of 2 seeds, bilaterally placed in brain stem, caused death
				0–1,100 r at 1 cm. in air	Total	Lower doses and dummy seeds allowed survival with graded lesions which increase proportionately with the dose
This Study	Monkey	Ta^{182}	Intracerebral	250 r at 2.0 cm.	4 days or less	With this dose and less no gross changes were seen
				591 r at 2.0 cm.	4 to 22 days	With this dose or more gross changes in meninges and in brain around "implant"
				3,097 r at 2.0 cm.	47 days and over	Clinical signs of hemiparesis appear. Increasing doses cause increasing severity of signs

In the animals sacrificed at short intervals after gamma irradiation, there was no definite change in the gross appearance. Upon histological examination, however, there were alterations in all parts of the cerebral cortex, but the basal ganglia, brain stem and cerebellum appeared essentially normal. The cortical change included loss of neurones and accompanying myelin sheath degeneration; the effect was judged to be primarily upon the neurone with myelin loss secondary to it. Microglial reaction was slight and only occasionally were compound granular corpuscles found about vessels. In these stages, astrocytic proliferation was mild. There were alterations in the blood vessels, especially those of the brain substance beneath the site of irradiation. The lesions, however, were distributed far more widely than the vascular changes, precluding the interpretation that the effect of gamma irradiation in our animals was wholly mediated by alterations in the blood vessels. It should be pointed out, however, that the completion of the dosage of gamma radiation from Ta^{182}, as used in the present

experiments, took from a few hours to seventy-two days. None of the results, therefore, can be regarded as equivalent to those obtained by the administration of the same dose in a matter of a few minutes from a much stronger source of gamma radiation. As has been pointed out elsewhere, the rate of administration of gamma radiation and roentgen radiation makes a great difference in the effect exerted by a given dosage upon tissue.

When brains from the monkeys surviving longest after the completion of gamma irradiation were cut in coronal planes, there were consistent and definite gross changes. The distinction between white and gray matter was less clear than usual in the cerebral cortex though the structures of the basal ganglia, brain stem and cerebellum were not altered. The most striking gross finding was the presence of small cystic areas in the white matter at the tips of the frontal and occipital poles; this was consistent in the animals surviving large doses of gamma radiation for several months.

Histopathologically, the changes were similar, qualitatively, to those seen in the group of short survivals but were quantitatively greatly intensified. The cystic changes at the poles were of the nature of infarctions resulting from extensive vascular damage. Throughout the cerebral cortex, the alterations in blood vessels were much more extensive and severe than they were in the preceding group. In spite of this, the extent and distribution of neuronal and myelin degeneration was too great and too diffuse to be explained wholly on the basis of the vascular occlusions seen.

A more extended discussion of the histopathological effects in the central nervous system, in the skin and in other viscera is being prepared for separate publication.

DISCUSSION

Biological responses to irradiation are dependent upon three factors: the nature of the radiation, the total dose and rate of irradiation, and the characteristics of the tissue irradiated. Gamma radiation alone is involved in these experiments, but it is well to remember that the qualitative effects of beta, gamma and roentgen irradiation are the same and are produced in the same way by ionization and secondary electron production at the site of absorption.[12]

The total dose of radiation is, of course, important, but the rate at which it is given may be equally important. While the exact limits of the effects of variations in rate are not known, it must be kept in mind that with isotope sources there is an appreciable change in the delivery rate of the radiation if the exposure time is near the isotope half-life or longer. For this reason the effects of the same total dose may differ if delivered by a roentgen-ray machine or an isotope source. Radiation energy is an important consideration, especially where the energies involved are low as in soft roentgen rays, but in the range of 0.8 mev. to 2 mev. (Ta^{182} gamma radiation is 94 per cent in this range) there is little change in the soft tissue linear absorption coefficient.

Dosage is usually expressed as radiation delivered, but this is unsatisfactory as it does not give an accurate description of what might happen in a tissue where the biologic effects of radiation are the result of energy absorbed. The amount of energy any tissue will absorb is dependent upon the nature of the tissue as well as the physical characteristics of the radiation. Absorption in bone is high and in fat low, with muscle between.

Spiers[85] has considered this problem at some length in calculating depth dose of roentgen rays, and demonstrates the real effect of the interposition of bone on depth doses which he attempts to calculate in terms of energy absorbed. In the present experiments the primary consideration is the effect on the brain in which the source is implanted which would seem to eliminate the difficulties presented by the heterogenous medium of the whole animal, but a brief consideration of the anatomy of the central nervous system will show that this is not the case.

The brain and spinal cord are composed of masses of white and gray matter, with the nerve cell bodies concentrated in the gray matter and the white matter made up of myelin-coated axis cylinders. Such a structure will not absorb radiation uniformly nor would the same effects be expected if it did, as a lesion in white matter is not necessarily equivalent to a similar one in the gray matter. In assessing the effects of radiation on the central nervous system, gross clinical changes are of minor importance as a relatively small lesion correctly placed is fatal[12] while relatively large volumes of brain tissue can be removed from certain areas with little effect.

Although the final evaluation of these experiments cannot be made at present it is of considerable interest to compare these observations with other reported results.

The comparison (Table II) of the roentgen-ray effects and isotope gamma radiation effects indicates that the high dosage rate of the lower energy roentgen rays results in damage at lower total doses. The recorded gross effects of single doses of roentgen rays to the cerebrum suggest that there is a threshold for acute effects around 4,000 r and about 2,500 r for delayed effects in both rabbits and monkeys. The work of Carty and Ray[54] gives a much higher figure for the threshold in dogs, but as they used much softer roentgen rays, the experiments are not really comparable. The results of experiments with radium are much less satisfactory. The dosages delivered by radium have never been delivered as fast as roentgen rays nor have the animals been followed as long. Only in the experiments of Pendergrass *et al.*[62] can any comparable effect be found. They showed in dogs that radium applied to the surface of the brain to give doses of 7,560 r at 1 cm. in twelve hours (10 r/min.) produced death and hemorrhage. Their threshold dose for clinical effects was about 6,000 r at 1 cm. in ten hours (10 r/min.) from a well filtered source. In the Ta^{182} series reported here, the threshold for hemiparesis seems to be about 3,500 r to the motor strip of monkeys over forty-seven days, or about 75 r per day. These dose differences in the clinical effects observed after irradiation by roentgen rays and by isotope gamma radiation are only qualitatively valid. The difficulty of accurately assessing the changes and the uncertainty of the dose delivered to the motor area introduce errors which invalidate quantitative statements.

The disparity between the isotope and roentgen radiation effects on the spinal cord are more striking than on the brain and are probably more accurate because of the ease of detecting damage to the spinal cord and the more similar relationship of the radiation source to the spinal cord than to the motor area of the brain. Davidoff *et al.*[23] found a threshold about 4,000 r (200 kv.; 58 r/min.) for delayed effects after irradiation of the spinal cord of monkeys. This is much less than the threshold dose of 11,000 r in dogs found by Pendergrass using radium (10 r/min.). Monkeys seem to be even more resistant to this type of irradiation. From Cairns and Fulton's[15] work with radon it can be calculated that a total dose of 94,140 r to the center of the spinal cord was required to produce a slight paraplegia in monkeys; however, this was first apparent in three days after about 39,000 r had been delivered. Under the conditions of the experiment, approximately 15,500 r (average 10 r/min.) were given the first day, 13,000 r (9 r/min.) the second, and 10,900 r (7.5 r/min.) the third day. Monkeys which received 71,820 r total, but only 11,900 (8 r/min.) the first day and 9,900 (7 r/min.) the second day never showed any clinical effects. Small doses of radiation do cause real lesions, as has been shown by Borison and Wang[12] who produced fatal lesions in the medulla of dogs by using small amounts of radon (678 r at 1 cm. in a total dose) which delivered only 113 r the first day (0.08 r.min.) and 93 r the second day.

The study of the effects of large doses of radiation will give a measure of the reserves of the various parts of the nervous system but for knowledge of the resistance

of cellular components the periphery of the large lesions must be carefully studied and, perhaps more important, the local effects of small graded doses of radiation should be more completely examined in all stages, early and late.

SUMMARY

1. Localized irradiation of the central nervous system has been carried out using tantalum 182 as a source. This produces a gamma radiation of about 1.1 mev. energy at the rate of 6.1 r/mc./hr. at 1 cm. in air. The doses used have ranged from a few roentgens to several thousand roentgens. Complete irradiation data have been given so that the dosages can be converted to units other than roentgens if it is desirable.

2. Gross and microscopic observations on a series of acute experiments on 18 monkeys are reported. The changes found were more extensive than could be accounted for by vascular damage alone, which suggests direct neuronal or glial effects.

3. An attempt has been made to collect the observations of others on the effect of gamma and roentgen radiation on the central nervous system. However, because of the differences in methods of reporting dosage, this has been only partially successful. There were great differences between dosage effects from isotope gamma radiation and roentgen radiation, but there are not enough data to assess the importance of such factors as radiation energy and dose rate.

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A STUDY OF THE IRRADIATION SYNDROME*

I. WATER, ELECTROLYTE AND NITROGEN BALANCES

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THIS investigation is concerned with water, electrolyte, and nitrogen balances in the irradiation syndrome, the relationship of these balances to each other, and their relation to water and electrolyte content of the various tissues of the body. The problem is complicated by the fact that many of the characteristic symptoms of irradiation sickness such as anorexia, fever, vomiting, diarrhea, infection, and possibly mineral-steroid alterations,[6,8,11,29,35] are in themselves conducive to water, electrolyte and nitrogen abnormalities.

RÉSUMÉ OF PREVIOUS WORK

Water and ionic alterations in the irradiation syndrome have been studied by many workers, but the results obtained have been variable, due to different species of animals studied and the diversity of methods employed. Particularly in human subjects have dissimilar observations been noted, probably because relatively few persons studied have had total body irradiation or uniform amounts of radiation, and because the depleted condition of many of these patients has tended to confuse the picture.

Blood potassium, sodium, and chloride have been reported as normal or as showing inconsistent changes in dogs[26,30,31,33] and rats.[3] Cameron and McMillan[4] found decreased plasma chloride inconstantly in humans. Pohle *et al.*[26] cited three authors who described in humans transient lowering of chloride immediately after irradiation, with a rise to normal shortly thereafter. Pohle could not confirm this observation in dogs. Kohn[20] observed rises and falls of chloride, sometimes phasic in character, in guinea pigs and in rats.

In Moon's[22] series of dogs subjected to large doses of roentgen radiation, there was a rise in blood potassium associated with a shock-like state. Bennett, Bennett and Howland[2] found a rise in serum radiosodium in rats, and a concomitant fall in urinary sodium. Painter[24] noted an increase in sodium space. Excretions of potassium, sodium and chloride were increased in rats during postirradiation days one to four according to Edelmann.[9] Bowers and Scott,[3] using radiopotassium and radiosodium, also in rats, found increased excretions of potassium in the urine, reciprocal decrease in urinary sodium, and increased potassium and sodium in diarrheal stools. Two authors[4,5] have reported sodium chloride retention in roentgen irradiated humans. On the other hand, Goldman[15] found a negative chloride balance, as did Ellinger[12] who incriminated the adrenal. An ionic balance study (in scope similar to ours) was done by Philips *et al.*[25] following large doses of nitrogen mustard in dogs.

There is a paucity of nitrogen excretion data in the literature. Hall and Whipple[16] noted increased excretion of nonprotein nitrogen after abdominal irradiation in dogs. Prosser[28] measured nitrogen balance in 8 dogs which received 200–400 r. These authors found nitrogen balance to be normal until a "late depression period" was reached, when a negative balance occurred greater than that observed in control animals starved to the same extent. Negative nitrogen balances have been noted in patients undergoing roentgen therapy.[15]

It has been stated (Prosser[28]) that loss of

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water through respiration probably is reduced after irradiation. Polydipsia and polyuria have been variously reported in both rats and dogs. France[13] observed increased plasma volume, thiocyanate space, muscle water, and total body water in rats and mice following moderate dosage of roentgen rays. Soberman *et al.*[31] found no consistent changes in the water space of dogs except for increased plasma volume. Various investigators[13,14,28,31] have commented on the relatively small change in blood volume despite the development of anemia; this was attributed to increase in plasma volume.

It will be noted in the sections which follow that some of the observations cited above have been confirmed by us, though others have not; and that answers appear to have been provided for some of the doubtful issues. We have endeavored to develop a unified and logical concept of the syndrome as a physiologic response to irradiation injury, attempting to segregate pure effects of irradiation from those secondary to anorexia, vomiting, diarrhea, infection, etc.

METHODS

Healthy, adult, mongrel dogs were used, females being preferred. The animals, dewormed and vaccinated against distemper, were observed for at least six weeks before irradiation. During this period basal studies were made. Whenever a new diet* was introduced, at least two weeks were allowed for equilibration.

A calculated tissue dose of 450–550 r was delivered to the dorsum of each animal which was snugly encased in an adjustable 3/8 inch plywood box. A 250 kv., 25 ma. roentgen-ray machine was used at 125 cm. from the bottom of the box.

We made balance studies of potassium, sodium, chloride, and nitrogen for eleven to fifteen days before irradiation, and thereafter throughout the postirradiation syndrome. Fecal excreta, collected in large covered jars over several day periods, were kept covered with alcohol and were acidified with H_2SO_4 to prevent loss of nitrogen. After drying and grinding, aliquots were taken for analyses. Urine, drained into flasks containing H_2SO_4, was collected at a definite time each day and was made up to 1,000 cc. with the distilled water used to wash the collecting pan. Quantitative recoveries of electrolytes and nitrogen were made in this manner. Vomitus could usually be collected as a separate uncontaminated sample, inasmuch as emesis occurred for only short periods following irradiation. Formed stools, collected in periods demarcated by carmine ingestion, were easily separated from the urine; and even mushy stools which passed through the wire-mesh floor of the cage remained in a small area on the collecting pan and could, as a rule, be taken up separately.

Water balance determinations were made on adult female dogs. Food and water were offered *ad libitum*. Only animals with stabilized weight were irradiated. Each day's water intake was measured, and to this amount was added water of food ingested and water of metabolism (taken as 20 per cent of the dry weight of the food). Inasmuch as it had been determined previously that fresh formed stools contained a nearly constant percentage of water, the dry weight of stool was utilized to calculate the water content. Urine, voided on clean paraffined pans, drained into flasks with a loss of 1 to 3 per cent of the total volume. In determining the total water available for respiratory loss, urine and fecal water was subtracted from the total intake, and to this was added the amount of weight lost. This calculation is based on the assumption that all of the weight lost was water—an assumption that is not entirely correct and introduces a small, unimportant error.

Total body water was measured by antipyrine,†[32] and plasma volume by means of Evans Blue (T-1824).‡[27]

Both stool and food were prepared for analysis by digestion with 4N H_2SO_4 to black gummy residues, following which they were ashed overnight at 500–550° C. The ash was dissolved in water with the aid of a few drops

* Two types of food were used: "Purina" dog chow in dry compressed pellets purchased on the open market, and a moist meat food specially prepared for us and packed in sealed cans by the Hill Packing Co., Topeka, Kansas. This latter food, ordered in large lots, was found upon analysis to be uniform in composition. It contained 10 per cent protein and 2 to 3 per cent fat.

† Generously supplied by Eli Lilly and Company.

‡ Contributed through the courtesy of Eastman Kodak Company.

of concentrated HCl and was made up to volume. Potassium and sodium measurements were made with a Beckman flame photometer. Chlorides in blood and urine were measured by the method of Sendrow as modified by Van Slyke and Hiller.[17] The Sunderman modification[34] of the method of Van Slyke was used for chloride analyses of stool and food. A correction factor (which remained constant) was necessary to correlate between the methods. Nitrogen was determined by the micro-Kjeldahl technique of Hiller,[18] except that the distillate was collected in boric acid and titrated with HCl.

CALCULATIONS

The calculations employed followed closely those of Elkington and Winkler,[10] and Darrow.[7] The external chloride balance, Cl_b, was used to determine the amount of extracellular fluid loss, E, by means of the formula $Cl_b/Cl_e=E$ (Cl_e being the concentration of chloride in extracellular fluid). Sodium excreted from extracellular fluid loss, Na_E, was approximated by multiplying the concentration of sodium in extracellular fluid, Na_e, by the volume of extracellular fluid: $Na_E=Na_e\times E$. The value Na_E was subtracted algebraically from the total external sodium balance, Na_b, to determine the excess excretion or retention of sodium in relation to that anticipated from chloride excretion. Potassium was assigned to the intracellular space only, inasmuch as corrections of the external balance for the amount derived from loss of extracellular fluid were negligible compared to the relatively enormous amounts derived from loss of intracellular space. Loss of cellular mass was calculated by subtracting extracellular fluid from weight loss. These calculations were simplified by the observation made by ourselves and others, that the concentrations of potassium, sodium and chloride do not change in plasma during the syndrome beyond normal diurnal variations. In making the calculations, it was assumed for convenience that chloride occupies an extracellular position only. Although that assumption is not entirely correct, the results obtained on that basis are believed to be sufficiently accurate to justify its use. The validity of the data obtained in this way was substantiated by the manner in which potassium excretion checked with nitrogen excretion, and by a direct study (to be reported in Part II of this investigation[21]) of electrolyte disturbances in individual tissues. Chances for error were greater in those calculations which depended on measurements of weight. For instance, calculated cellular mass loss included not only the loss of water, ion, and nitrogen-rich tissue, but also loss of fat and hair, and errors due to variability in contents of intestines and bladder.

RESULTS AND DISCUSSION

Typical hemorrhagic syndromes were produced which, as a rule, resulted in death within three weeks. Anorexia was variable in degree and extent, being delayed and less pronounced in animals which ingested palatable meat food, as compared to those which were kept on checker diet. The meat diet was often taken in normal quantities until a day or two before death. Fever occurred with the onset of anorexia. Vomiting was usually observed to occur once in the first twenty-four hours after irradiation. Mushy rather than frank diarrheal stools were the rule. At times there was a bloody mucoid discharge from the rectum; otherwise external bleeding was limited to occasional hemorrhages from the uterus. No gross infections were noted at autopsy, but ulcerations, petechiae and ecchymoses of the oral and nasal mucous membranes were seen, as well as petechiae and superficial ulcerations in the stomach, in the ileocecal area, and (inconstantly) throughout the rest of the intestinal tract. Petechiae and ecchymoses were also observed in the retroperitoneal area, heart, lungs and periadrenal fat.

Water Balance. Total body water was reduced after irradiation in most of the animals. It had been observed that *in health* plasma volume bears a constant relation to total body water. This relationship was much more constant and seemed to be more logical than any relation between plasma volume and body weight. As might be anticipated, studies on obese animals profited most from this observation. *As the irradiation syndrome progressed,* however, plasma water did not participate in total body water reduction, so that in the end plasma constituted an abnormally large proportion

TABLE I

COMPARATIVE BALANCE STUDIES BETWEEN IRRADIATED ANOREXIC DOGS AND THEIR PAIR-FED CONTROLS

Group	Dog	Duration of Anorexia	Diet	Changes in Extracellular Fluid Volume		Changes in Cell Mass	K Balance during Anorexia	Total K Balance Postirradiation	Fate of Animal
				Based on Cl bal.	Based on Na bal.				
		Days		Kg.	Kg.	Kg.	mEq.	mEq.	
I	Pair-fed	5	Moist, high-prot.	−0.45	−0.58	−0.65	− 44	− 84	
	Pair-fed	5	Pellet	−0.31	−0.42	−0.94	− 56	− 60	
	Irradiated	5	Pellet	−0.65	−0.61	−1.07	−106	−124	Died
II	Pair-fed	7	Moist, high-prot.	−0.57	−0.44	−1.2	− 73	− 82	
	Irradiated	7	Moist, high-prot.	−0.25	−0.35	−1.45	−161	−207	Died
III	Pair-fed	4	Moist, high-prot.	−0.22	−0.23	−0.38	− 30	− 54	
	Irradiated	4	Moist, high-prot.	−0.38	−0.34	−0.46	− 55	−110	Died
IV	Pair-fed	5	Pellet	−0.74	−0.57	−1.08	− 97	− 97	
	Irradiated	5	Pellet	−1.91	−1.48	−1.64	−144	−144	Died
V	Pair-fed	7	Moist, high-prot.	+0.05	+0.24	− <0.1	− 8	+ 6	
	*Irradiated	7	Moist, high-prot.	−0.09	−0.36	−0.15	− 14	− 23	Survived
VI	Irradiated	3	Moist, high-prot.	−0.22	−0.28	−0.75	− 83	−124	Died
VII	Irradiated	8	Moist, high-prot.	−0.80	−1.43	−2.5	−153	−179	Died

* This animal's anorexia reduced food intake to one-third of normal.

of the total water.

Part of the total water reduction may be attributed to loss of water-rich tissue from decreased food intake, and to a lesser extent to breakdown of radiosensitive tissue. Since plasma (and blood) volume and tissue water remained relatively constant, any remaining loss of water must have occurred diffusely from interstitial fluid. This concept is borne out by electrolyte studies (*vide infra*).

The reason why interstitial fluid was depleted became apparent after a study of water balance. Water balance was affected by the various degrees of starvation in our normal animals, and of anorexia in our irradiated animals. Both groups were offered water *ad libitum*. When food was withheld, or, when offered, food was not eaten, the amounts of water ingested decreased appreciably. Urine output remained unaltered, however, or was only moderately decreased, and what might be considered a maximum reduction was never observed. When the animals did not drink enough to meet basal needs, water requirements were met by depletion of the body's own water stores. A large portion of this water was

derived from cellular breakdown of starvation, the remainder coming from the interstitial space. Large amounts of sodium and chloride were excreted in consequence. Table I indicates the amounts of interstitial water and cellular mass lost by irradiated animals as compared with their pair-fed controls, calculated on the basis of chloride excretion. The large amounts of both modalities excreted by the irradiated group were due presumably to increased metabolism from fever, to breakdown of radiosensitive tissue, and possibly to oligodipsia.

In calculating water losses, weight loss had to be taken into consideration, since that represented available water. Loss of water from the respiratory tract varied considerably in both healthy and irradiated dogs eating a full diet (range of water loss: 0.77 to 1.4 gm. per kg. per hr.), whereas healthy starved or irradiated anoxic animals showed much less variation (range: 0.57 to 0.87 gm. per kg. per hr., with a value of about 0.85 for the majority of the dogs.) It would appear that in starved and anorexic animals a fairly uniform basal state of respiratory water output was established, which did not differ greatly from animal to animal, as was true also for relations among ions excreted (*vide infra*). Indeed, the variations which we observed might have been even less had water losses been expressed in terms of total body water or pulmonary exchange of water, rather than in the more conventional terms of body weight. Also, during control periods our animals doubtless lost considerable amounts of respiratory water from excitement, playfulness, panting, etc. It is noteworthy that irradiated dogs lost more *total body* water than did their pair-fed partners, although losses from the respiratory tract were the same in healthy and in irradiated animals under similar conditions of environment, activity, and food intake.

Clinically, it appears that water intake is a function of amount of food ingested, as well as a function of metabolic need. Water consumption is reduced in both enforced starvation and irradiation anorexia. It is probable that under these circumstances water lost from the respiratory tract represents not only water taken from the extracellular compartment (which drinking would replace) but also water obtained from starvation breakdown of tissue.

Weight Loss. Prior to anorexia, irradiated animals and their pair-fed partners lost approximately equal amounts of weight (average: 0.4 per cent of the original body weight per day), but after the appearance of anorexia, irradiated animals lost weight more rapidly than their pair-fed counterparts (2.6 per cent per day as compared with 1.5 per cent per day). Total weight losses in 5 irradiated and 5 pair-fed nonirradiated dogs measured: 15.7 *vs.* 11.6 per cent; 8.0 *vs.* 4.7 per cent; 20.5 *vs.* 9.0 per cent; 12.8 *vs.* 4.3 per cent; and 17.0 *vs.* 9.0 per cent. Anorexia and resultant weight losses were delayed and less pronounced in irradiated animals on palatable meat diet, in contrast to those kept on dry pellet diet. When irradiated dogs consumed normal amounts of food,* as little as 3 per cent of the original body weight was lost in twelve days.

External Balance. The excretion data obtained on 6 dogs following irradiation are shown in Table II. These animals all had been well equilibrated prior to irradiation in respect to weight, nitrogen balance, and electrolyte balance. Before the onset of marked anorexia, chloride balance was negative in only 2 instances, while both sodium and potassium were in negative balance in every instance. After anorexia all three ions were in negative balance. The degree of negativity is shown in Table I in which irradiated animals are compared with their pair-fed partners. As might be anticipated from weight losses, the irradiated dogs lost the larger amounts of both potassium (cellular mass) and chloride (extracellular fluid).

From the total data on all the animals,

* Thus, one animal which ate fully until the day of death lost only 0.3 kg. over the entire twelve day syndrome. Ion loss was then proportionately low: K, −11 mEq.; Na, −11 mEq.; Cl. +17 mEq.

TABLE II

EXTERNAL IONIC BALANCES FOLLOWING IRRADIATION

Dog No.	Period of Observation	Food		External Balance			Weight Changes			Ratio K/CML*
		Type	Intake	K	Na	Cl	Total body weight	Extracellular fluid	Cellular mass	
	Days			mEq.	mEq.	mEq.	Kg.	Kg.	Kg.	
30	6	Pellet	Partial anorexia	− 18	− 5	+ 11	−0.50	+ 0.09	−0.59	30.5
	5		Total anorexia	−106	− 96	− 77	−1.72	−0.648	−1.07	100
(Total)	11			−124	−101	− 66	−2.22	−0.558	−1.66	75
36	5	Pellet	Total anorexia	−144	−234	−225	−3.55	−1.91	−1.64	89
20	12	Moist, high-prot.	Full intake	− 41	−121	+ 18	−0.48	+0.152	−0.63	65
	3		Total anorexia	− 83	− 44	− 26	−0.97	−0.221	−0.75	111
(Total)	15			−124	−164	− 8	−1.45	−0.070	−1.38	89
21	12	Moist, high-prot.	Pre-anoxic	− 26	− 39	+ 14	−0.35	+0.116	−0.47	58
	8		Total anorexia	−153	−188	−107	−3.4	−0.905	−2.5	61
(Total)	20			−179	−227	− 94	−3.75	−0.789	−2.97	60†
27	11	Moist, high-prot.	Pre-anoxic	− 46	− 34	− 36	− 0.8	−0.307	− 0.5	93
	7		Total anorexia	−161	− 55	− 30	− 1.7	−0.254	−1.45	111
(Total)	18			−207	− 89	− 66	− 2.5	−0.561	−1.95	106
29	7	Moist, high-prot.	Partial anorexia	− 55	− 78	− 69	−1.11	−0.583	−0.53	104
	4		Total anorexia	− 55	− 53	− 45	−0.84	−0.377	−0.46	119
(Total)	11			−110	−131	−114	−1.95	−0.960	−0.99	111

* Ratio of potassium loss (in mEq.) to Cellular Mass Loss (in Kg.)

† This value was low because the animal lost 20 per cent of its total blood volume in hemorrhages from the uterus. Included in the derived data, it made calculations for E too low and for CML too high, lowering the K/CML ratio.

it was calculated that 10.6 kg. of cellular mass was lost altogether, and that there was a collective negative potassium balance of 911 mEq. That is to say, on the average, 86 mEq. of potassium were lost for each kilogram of calculated cellular mass loss. This value may be compared with our observed value of 90–95 mEq. for muscle. Indeed, the only low value (61 mEq.) obtained was in a dog which bled profusely from the uterus. In this instance, the external fluid balance received from whole blood a fluid less rich in chloride than the fluid derived from the interstitial compartment (80 mEq. *vs.* 107 mEq.). The hemorrhage had the effect of making the calculations of loss of extracellular fluid too low, and hence the calculated values of potassium per kilogram of cellular mass loss were too low also.

In terms of anticipated values for potassium, the data were less variable during anorexia alone than during the entire post-irradiation period. Sodium and chloride were also excreted during anorexia in relative amounts which approximated the proportions normally seen in extracellular fluid. As was true for water balance (*vide supra*) ion balances during anorexia approached a basal state of metabolism. Another influential factor, however, was that the relatively large weight losses tended to reduce errors of weighing upon which the calculations depended, and at the same time the total amount of ions to be measured were increased. The correspondence between measured and anticipated potassium values enhanced the feasibility of using chloride balance as an index of extracellular change.

When similar calculations were used for nitrogen, the loss was observed to be 34.7 ± 5.3 gm. per kg. of cellular loss. This mean is close to the theoretical value of 36 gm. of nitrogen per kg. of muscle.

Studies were also made of the relation of potassium excretion to nitrogen excretion in irradiated dogs. To simplify balance cal-

culations, it was assumed that all potassium and nitrogen were derived from tissue breakdown, and minor quantities of these substances occasioned by loss of extracellular fluid were ignored. Hemorrhage contributed small amounts of potassium and large amounts of nitrogen to the excretion data; they were taken into account in making the calculations. In most instances the observed ratio (2.75 ± 0.3) of potassium balance (in mEq.) to nitrogen balance (in gm.) approximated that seen in the tissues (our value for muscle was 2.8). This relationship was more accurate and informative than the relation of either potassium or nitrogen to weight loss or to calculated cellular mass. Urine K/N ratios tended to parallel the nutritional status of the animal. During the control periods, they were similar to that of food ingested (urine 1.49 ± 0.09; food 1.45); after irradiation, even with normal food intake, the urine K/N ratios may have risen slightly (1.63 ± 0.11); with anorexia they approached 2.8 (2.68 ± 0.35). Similar K/N ratios were observed in irradiated and control dogs fed equivalent amounts of food. These ratios approached 2.8 slowly after the development of anorexia in irradiated pellet-fed animals, inasmuch as nitrogen from the food that had been ingested continued to be excreted in urine for two days after the animals stopped eating. A similar delay was noted in healthy animals purposely starved after having been on a pellet diet, which implied that the slow absorption and excretion of this food nitrogen was not a result of irradiation of the gastrointestinal tract. Animals eating moist meat food developed 2.8 ratios promptly after the appearance of anorexia, which indicated comparatively rapid and complete intestinal absorption. Daily excretions of fecal nitrogen were the same for animals on both sorts of diet. There was no increase in nitrogen excretion by this route even in the presence of normal food intake.

Sodium balance (Table II) was always negative after irradiation in spite of relative retention of chloride in some instances. This finding precluded the possibility that excreted sodium was derived entirely from the extracellular space, although following anorexia its relation to excreted chloride was approximately that found in extracellular fluid. It was interesting to correlate sodium excretion with muscle sodium as the syndrome progressed. Muscle sodium was found to be depleted in nearly every animal shortly after irradiation. This was not easy to explain. It seemed unlikely that sodium would appear in the external balance in larger amounts than would be expected from the chloride balance, since conditions during the syndrome in dogs did not seem to be conducive to muscle sodium loss. Sodium loss in vomitus was small. The mushy stools contained more electrolytes than normal (potassium 2 times normal, sodium 1.5–5 times normal, chloride 1.2–3 times normal), but the stools were not frequent enough nor bulky enough to account for the sodium depletion; in particular, they would not account for selective depletion of sodium. Furthermore, in these situations of abnormal electrolyte loss, it was noted that renal excretion of electrolytes was usually reduced in proportion. Thus, the defenses of the kidney also tended to oppose selective obligatory loss of sodium. And finally, none of the body tissues was found to become sodium-rich without concomitant acceptance of chloride. It would be informative in a study like this to administer radioactive sodium and trace its movements after total body irradiation.

INTERPRETATION AND CONCLUSIONS

Total body water was reduced following roentgen irradiation as a natural response to oligodipsia, decreased food and water intake, and consequent loss of tissue mass. Obligatory evaporative water loss is believed to have been essentially the same for starved healthy animals and anorexic irradiated animals, although it is possible that an occasional irradiated animal, because of reduced activity, had decreased respiratory water loss. In the face of reduced intake and normal output of water,

it is concluded that water for respiratory loss was met by tissue breakdown and attendant depletion of extracellular fluid. Tissue water analyses showed that dehydration was not present to any important degree.[21] The normal K/N ratios in our balance studies are another indication that significant dehydration was not present.[36] Part of the water excreted in excess of the amount anticipated from tissue breakdown was probably lost as a result of fever *per se*.[23] The extracellular fluid loss also accounts for the large chloride excretions observed, and it is not necessary to incriminate irradiation. This conclusion is supported by the absence in our animals of any acid-base disturbance or shift of chloride ions; on the contrary, chloride concentration in the major tissues of the body[21] and in serum remained remarkably constant. It is interesting that plasma volume increased in the face of extracellular fluid loss, although such increases are consistent even with appreciable dehydration.[19]

Our external balance studies showed that irradiated animals lost more electrolytes and nitrogen than did healthy animals given equivalent food intake. Potassium and nitrogen appeared to be excreted in the same ratio as obtains in tissue. Chloride, insofar as it is a measure of extracellular fluid, maintained its integrity. Sodium was a less reliable measure of extracellular fluid since, in the external balance, it did not maintain the relation to chloride normally seen in extracellular fluid. Sodium is the possible exception to the conclusion that significant depletion of water (in the sense of dehydration) did not occur, or that depletion of electrolytes (in the sense of altered relation to each other) was not observed. Our failure to detect retention of sodium, as Bennett[2] did, was probably due to the fact that we employed a different species of animal and did not use radiosodium. Of course, radioactive ions measure different functions, and anorexia can affect exchange and excretion of such ions independently of balance studies. Such observations have been made in connection with potassium in anorexia.[1] Edelmann[9] who did not use isotopes, found increased sodium excretion in rats. In a study paralleling ours, Philips and associates[25] observed the effects of nitrogen mustard poisoning in dogs. Although histologic and chemical changes were noted which were similar in some respects to those seen in the roentgen irradiation syndrome, these investigators also reported increased water intake, inconstant pronounced relative retention of sodium, and excretion of more potassium than could be accounted for by nitrogen studies. These latter findings are in contrast to ours. The conclusions of these workers in regard to loss of extracellular water are similar to ours, however, in that the loss is attributed to a considerable extent to reduced water intake, and not primarily to the injurious agent *per se*.

We have concluded that after irradiation our animals were able to handle large amounts of ingested protein, very much as they did before irradiation. Excretion of nitrogen in stools was not increased, no delay in nitrogen absorption was detected, and body weight was well maintained when adequate food was ingested. The implication is clear that, given a high protein diet, the irradiated dog is able to convert protein into energy and maintain caloric balance. It follows, from a therapeutic standpoint, that a palatable diet should be offered with the expectation that it will be ingested, absorbed, and metabolized in a virtually normal manner. Although increased catabolism results in abnormal losses of weight, water, electrolytes, and nitrogen, the irradiated animals do not become dehydrated appreciably, nor do they exhibit ionic imbalance induced by irradiation beyond that which can be accounted for by anorexia, variable degrees of vomiting and diarrhea, fever, and infection.

SUMMARY

A study has been made of effects of acute total body irradiation upon water, electrolyte, and nitrogen balances in dogs in which typical hemorrhagic syndromes were produced.

A brief résumé of previous work done on this subject is presented.

The main abnormalities observed by us were:

(1) Reduced total body water without significant dehydration.

(2) Small decreases in blood volume, the decreases incident to reduction of red cell mass being countered by moderate increase in plasma volume.

(3) Decreased water intake with nearly normal water losses, the resultant water deficit being compensated for mainly through tissue loss and diffuse loss of extracellular fluid.

(4) Weight loss, more pronounced in animals on dry pellet diet than in those on palatable meat-rich diet, due to delayed onset of anorexia in the latter group.

(5) Negative sodium and potassium balances throughout the syndrome; inconsistently negative chloride balance before the onset of anorexia, and consistently negative chloride balance after anorexia.

(6) Increased K/N balance ratio which, after anorexia, approached the K/N ratio of muscle.

(7) No evidence from external balance studies of acid-base disturbance, or of gross depletion or internal shift of potassium, sodium, or chloride.

When irradiated animals were offered moist, palatable, high-protein diet, anorexia was delayed, often until shortly before death. Prior to anorexia, digestion, absorption, and metabolism of nitrogen proceeded in a nearly normal manner. Therapeutic implications of this observation are obvious.

Indeed, most of the observed effects of irradiation upon water, electrolyte, and nitrogen balances can be accounted for largely on the basis of anorexia, oligodipsia, vomiting, diarrhea, fever, infection, etc., and need not be attributed to any significant degree to the primary effects of irradiation itself.

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EDITORIALS

OSTEOPOROSIS: THE POTENTIALITIES AND LIMITATIONS OF ITS ROENTGENOLOGIC DIAGNOSIS

MOST radiologists are aware that bone is not an inert mass, but is composed of living tissue which participates in all vital processes of the body and is responsive to physiologic and pathologic alterations. As a normal physiologic process new bone is laid down constantly while old bone disintegrates. Seen in this light of a dynamic balance between bone formation and bone resorption, roentgen examination of the skeleton gains new significance in that it is capable of revealing metabolic, hormonal, and other disturbances that interfere with this balance.

If we regard the skeleton as the mineral storehouse of the body, we can readily understand that it may be attacked in endocrine and metabolic disorders in which there is a disturbance of mineral metabolism. But only in recent years has it been realized that the most important part of bone is not the inorganic portion but a protein matrix in which the calcium salts are precipitated. This matrix is a product of the osteoblasts. Albright[1] has consistently pointed out that certain diseases of the skeleton are caused by disturbances of the organic bone matrix and that in these entities the involvement of the bone minerals is secondary to deficiencies of the organic component.

Diseases in which the primary disturbance concerns the calcium and phosphorus metabolism have been classified under the general heading of bone malacia. Here demineralization of the skeleton develops because insufficient calcium and phosphates are available for deposition in the normally formed bony matrix, and repair of the daily wear and tear of the skeleton becomes impossible.[16] In microscopic sections of osteomalacic bone non-calcified bony matrix appears as broad osteoid borders surrounding the trabeculae.[16] To this group belong nutritional and other disturbances such as rickets and osteomalacia, sprue and celiac disease, and renal deficiencies, known under the general heading of osteonephropathies.[8]

On the other hand bone atrophy, the primary cause of which is a disturbance in the formation of the organic matrix by the osteoblasts, is designated as osteoporosis.[1] To this group belong bone atrophy of disuse during immobilization; osteoporosis in hypovitaminosis *C*, in starvation and malnutrition, in hyperthyroidism; osteoporosis due to imbalance or deficiencies in the steroid hormones, as in senility, in the postmenopausal state, in Cushing's syndrome, and during ACTH and cortisone treatment.[1,8,16]

Finally, demineralization may be due to increased bone destruction as the result of excessive osteoclastic activity, such as occurs in hyperparathyroidism.[16]

Schinz and co-authors[15] in their text have pointed out that it is impossible to distinguish roentgenologically between these different forms of demineralization of the skeleton and apply the term "osteoporosis" to all forms of bone rarefaction, irrespective of whether the deficiency is due to absence of calcification of newly formed bone, to insufficient osteoblastic activity or to increased activity of the osteoclasts. Ritvo,[14] in his recent book, calls attention to marked differences between the roentgenologic and pathologic concepts of osteoporosis and defines it for the radiologist as a deficiency of calcium which manifests itself as a rarefaction of bone.

The first roentgen sign in the acute stage is a general increased translucency of the bone. The structure appears hazy and blurred. Within the spongy part we see irregular areas of reduced density. The trabeculae are no longer sharply defined as in the normal, but fade into one another. Later, as decalcification progresses, or in primary chronic cases, blurring disappears, the bone texture becomes sharp, the trabeculae well defined, but their meshwork is wider than normal and the individual lamellae are thinner. At the same time the cortex becomes thinner and lamellar. In extreme cases the cortex may become very narrow and appear as if drawn with a fine pencil; the trabecular structure may be almost invisible. The bone takes on a glass-like appearance. We may find transitions between the first and second stage and mixed pictures. The appearance of some hypertrophic thickened lamellae in places where they have important static functions, may serve as a further sign of a chronic case.[10]

In regards to the limitations and accuracy of the roentgenologic method in the diagnosis of osteoporosis, the following questions may be asked:[10] (1) What degree of demineralization must be present before it can be diagnosed in the roentgenogram? (2) Is the amount of decalcification necessary for diagnosis the same in all bones and the same in all parts of a given bone? (3) Between what degrees of decalcification can we differentiate on the film? These questions are, of course, of the greatest clinical importance since roentgenologic demonstration of osteoporosis is often the only clue to its clinical diagnosis.

The problem has been approached experimentally by several investigators,[2,7,10] who subjected macerated human bone to increasing chemical decalcification by means of nitric acid, simultaneously roentgenographing the bone at each stage. Quantitative chemical analysis furnished information on the amount of calcium, removed successively. By determining the calcium in the ashed residue, it was possible to express the calcium removed at each step in percentages of the total calcium present in the bone initially and correlate this with the roentgenologic appearance of the gradually demineralized bone. On the basis of their experiments these investigators[2,7,10] are in essential agreement, that it requires a minimum calcium loss of 30 per cent, possibly up to 50 or 60 per cent, before a rarefaction can be detected roentgenologically. The obscuring influence of soft tissues is pointed out as is the increased difficulty in establishing a diagnosis if initial normal control films are absent. Lachmann and Whelan[10] use the roentgenogram of an osteomalacic rib and compare it with a chemically decalcified rib, stating that the calcium loss in the malacic rib probably amounts to 60–70 per cent. On the basis of their experiments they point out that the amount of decalcification necessary for diagnosis varies considerably in different bones and in different parts of the same bone depending on the structural, composition of the bone. Bones with a great amount of spongy texture and relatively thin cortex give the earliest results. Under very favorable experimental conditions differences in calcium content of approximately 7 per cent seem to be recognizable if serial studies on the same bone are made. In actual clinical cases of osteoporosis it may take years until appreciable roentgenographic abnormalities can be noted.[17] By the same token it may also require a period of years before a therapeutically induced improvement in the calcium content of the bones would be revealed on the roentgenogram.

In recent years a number of investigators have approached the problem of the roentgen diagnosis of osteoporosis from a different angle. Their research is quite promising and, if successful, may establish a sounder and more accurate basis for the diagnosis of mineral deficiencies even in marginal cases. Everybody agrees that the present method which compares the skeletal film with vague visual recollections of past cases is highly subjective and un-

scientific.[5] Thus the need for objective, quantitative evaluation of bone mineralization from roentgenograms of living human subjects and experimental animals has long been realized.

For a number of years Mack and her co-workers[11,12] at Pennsylvania State College, School of Chemistry and Physics, and later Brown and his co-workers,[3,12] in the Bone Density Research and Evaluation Center of the same institution have set themselves the task of developing a precise method for quantitative roentgenographic determination of bone mineralization. Apparatus was designed with which it is possible by means of objective photometric technique to evaluate the mineral content of bones from the roentgenogram of the living subject. In order to avoid the difficulty of locating precisely on the film the same point for comparative serial studies in the same or in different subjects, a scanning or tracing technique was adopted in which a stationary beam of light passes through a portion of the roentgen-ray film. This film moves at a standard speed over a standard tracing path on the roentgenogram, *e.g.*, diagonally through the calcaneus between two reproducible land marks. The amount of light transmitted through the image of this bone slice is recorded and measured by a densitometer. The accuracy of the photometric scanning technique depends upon the validity of the assumption that the degree of blackening of the roentgenographic image, *i.e.*, its photographic density is related in a known manner to the mineral content of the bone roentgenographed, and furthermore that through the use of an ivory step wedge of known dimensions, placed on the film adjacent to the bone, corrections can be applied for variations in exposure and photographic processing.[12] Thus, in each case a specific calibration curve is obtained from the image of the graduated step wedge. The densitometric tracing of the roentgenogram of the bone is computed automatically in terms of the calibration curve of the step wedge by means of recording, integrating and counting devices. The transradiated bone volume is determined after allowance has been made for the overlying soft tissue mass. The result of the densitometric evaluation of the bone is expressed either in terms of the average equivalent ivory thickness or as grams of bone ash per cubic centimeter of bone.

Paralleling the research done by Mack and Brown and their co-workers,[3,11,12] other investigators have also approached the problem of objective quantitative evaluation of bone mineralization.[4,6,9,18] They all call attention to pitfalls in the use of the method. The soft tissues surrounding a bone to be measured are a definite source of error. Their mass must be determined by special computations to give correct figures for bone density. Consequently, most of the applications of the method have been limited to phalanges, radius, ulna, and calcaneus, where soft tissue corrections can be made quite accurately. According to a recent publication by McFarland[13] from the Pennsylvania group, bone density determinations from films of approximately 1,200 persons of all ages and both sexes revealed a 2–1 range of variation. "Normal" adults fall within approximately ten groups of bone mineralization. It is claimed by the author that reproducibility of the measurement is on the order of a 5 per cent variation. This is somewhat surprising since it seems difficult to place the bone in exactly the same position in re-examination, and the slightest rotation would be apt to produce differences in terms of bone density. Another source of error might be the distance of the wedge from the center of the film where the bone is placed, with resulting differences in absorption of roentgen rays by the object and the step wedge control.

So far, the reliability of this method has not been confirmed by other investigators on the basis of independent studies on a broad scale; however, if photometric evaluation of bone mineralization according to the designed procedure should prove to be a reliable test, the importance of the

method can hardly be overestimated. Nutritional studies on mineral metabolism could be undertaken experimentally, without necessitating the sacrifice of the animals during the experiment for chemical determination of the mineral content of bones. Bone density measurements would prove to be an important clinical tool in the diagnosis of deficiency states such as might occur in pregnancy, intercurrent illness, endocrine disturbances and dietary deviations.[12] So far, few clinical reports have been published by the Pennsylvania group. In a recent discussion (1953), Mack claimed that changes could be noted in a single day upon animals in which the calcium intake was greatly altered.

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WM. EDGAR REILEY
1882-1955

WM. EDGAR REILEY died at his home in Clearfield, Pennsylvania, on June 5, 1955. He had been in failing health for the past few years and was obliged to resign his position as Chief of the Department of Radiology at the Clearfield Hospital in December, 1953.

Born in Hanover, Pennsylvania, Dr. Reiley was the son of The Reverend McKendree Reiley, a former pastor of the Fifth Avenue Methodist Church in Altoona, Pennsylvania, and of Fannie (Baker) Reiley.

He graduated from the Altoona High School in 1902 and from the Southern Homeopathic College of Baltimore, Mary-

land, in 1907. After a year's graduate work in New York, he started practice in Clearfield, where he was associated with the late Dr. Samuel J. Waterworth. Later he resumed graduate work in radiology at Johns Hopkins University in Baltimore. Sincere and enthusiastic about his profession, he became well informed in all branches of radiology.

Dr. Reiley was one of the principal founders of the Pennsylvania Radiological Society. To him went most of the credit for the successful growth of the organization in its early days and for its continued expansion. He was twice President of the Pennsylvania Radiological Society and was its Secretary-Treasurer for a number of years. Other societies of which he was a member are the American Medical Association, Medical Society of the State of Pennsylvania, Clearfield County Medical Society, American Roentgen Ray Society, Radiological Society of North America, a Fellow of the American College of Radiology and a Diplomate of the American Board of Radiology.

Dr. Reiley is survived by his wife, the former Alma Litz of Clearfield, Pennsylvania; two daughters, Mrs. Harry Lawler of Billings, Montana, and Mrs. Meade Stapler of Riverdale, New Jersey; one son, James L. Reiley of Elliotsburg, Pennsylvania; one brother, Henry Baker Reiley of Somerset, Pennsylvania; and three sisters, Mrs. James W. Lother of Altoona, Pennsylvania, Mrs. L. L. Owens of Altoona, Pennsylvania, and Mrs. William Eddy of Carlisle, Pennsylvania.

G. D. Bliss, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

ATLANTA RADIOLOGICAL SOCIETY

At a recent meeting of the Atlanta Radiological Society, the following new officers were elected: *President*, Dr. H. Stephen Weens; *Vice President*, Dr. Ernest G. Smith, Jr., *Secretary-Treasurer*, Dr. Charles M. Silverstein, 3254 Peachtree Road, N.E., Atlanta, Georgia.

BROOKLYN RADIOLOGICAL SOCIETY

The Brooklyn Radiological Society recently elected the following new officers: *President*, Dr. A. L. L. Bell; *Vice President*, Dr. Daniel Butera; *Secretary-Treasurer*, Dr. Theodore Kamholtz, 152 Clinton Street, Brooklyn 1, New York. The Brooklyn Radiological Society meets the first Thursday of the month, October through May.

CLEVELAND RADIOLOGICAL SOCIETY

At the last meeting of the Cleveland Radiological Society, the following new officers were elected: *President*, Dr. H. F. Inderlied; *Vice President*, Dr. Emmett J. O'Malley; *Secretary-Treasurer*, Dr. Arthur S. Tucker, 2020 East 93rd Street, Cleveland 6, Ohio.

EASTERN CONFERENCE OF RADIOLOGISTS

The Eastern Conference of Radiologists will meet in Baltimore, Maryland, on Thursday, Friday, and Saturday, March 15, 16, and 17, 1956, at the Lord Baltimore Hotel.

This informal organization has been meeting annually since before 1915. Meetings are held in Boston, Baltimore, New York, Philadelphia and Washington in that rotation. The New England Roentgen Ray Society, the Radiological Section of the Baltimore City Medical Society, the New York Roentgen Ray Society, the Philadelphia Roentgen Ray Society and the Radiological Section of the District of Columbia Medical Sciety act as hosts.

There is no formal membership and the host society plans its own program each year. Continuity is assured by a permanent secretary and an annual meeting of delegates. There are no commercial exhibits. Commercial representatives, however, may register and sponsor activities either before or after the meeting but will not be included in the program.

Advance registration may be made by writing to Dr. Richard B. Hanchett, 705 Medical Arts Building, Baltimore 1, Maryland.

OHIO STATE RADIOLOGICAL SOCIETY

At the annual meeting of The Ohio State Radiological Society, the following officers were elected for the ensuing year: *President*, Dr. George R. Krause, Cleveland, Ohio; *Vice President* and *President-Elect*, Dr. Donald English, Lima, Ohio; *Secretary*, Dr. John R. Hannan, 10515 Carnegie Avenue, Cleveland 6, Ohio; *Treasurer*, Dr. Paul Jones, Zanesville, Ohio. The next annual meeting will be held at the Deshler-Hilton Hotel in Columbus, Ohio, May 12–13, 1956.

PENNSYLVANIA RADIOLOGICAL SOCIETY

At the annual meeting of The Pennsylvania Radiological Society held in Reading, Pennsylvania on May 21, 1955, the following officers for the year 1955–1956 were elected: *President*, Dr. William T. Rice; *President-Elect*, Dr. James M. Converse; *First Vice President*, Dr. Jesse T. Littleton, III; *Second Vice President*, Dr. John F. Maurer; *Secretary-Treasurer*, Dr. Walter P. Bitner, 234 State Street, Harrisburg, Pennsylvania.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

At the annual meeting of the Rocky Mountain Radiological Society held in Denver, Colorado, on August 18, 19 and 20, 1955, the following officers were elected for the coming year: *President*, Dr. Maurice D. Frazer, Lincoln, Nebraska; *President-Elect*, Dr. John S. Bouslog, Denver, Colorado; *First Vice President*, Dr. C. S. Hatchett, Jr., Amarillo, Texas; *Second Vice President*, Dr. Ralph C. Moore, Omaha, Nebraska; *Secretary-Treasurer*, Dr. John H. Freed, 4200 East 9th Avenue, Denver 20, Colorado.

* The list of Meetings of Radiological Societies appears in the September, 1955, issue of the Journal, and will be published in the November number.

SOCIEDAD ECUATORIANA DE RADIOLOGIA Y FISIOTERAPIA

The following officers were named recently by the Sociedad Ecuatoriana de Radiologia y Fisioterapia for the year 1955–1956: *President*, Dr. German Abad Valenzuela; *Vice President*, Dr. Mario Hinojosa Cardona; *Secretary*, Dr. Enrique Ortega Guzmán, Casilla 4719, Guayaquil, Ecuador; *Treasurer*, Dr. Olga Seminario Vergara.

DUKE UNIVERSITY RECEIVES JAMES PICKER FOUNDATION GRANT

The James Picker Foundation has announced the award of a grant to the Duke University School of Medicine in support of the studies of Dr. Robert J. Reeves on the effects of roentgen irradiation upon digestion and absorption of materials in the gastrointestinal tract by means of radioactive tagged compounds and correlative roentgenological studies. This grant was made on recommendation of the Committee on Radiology, Division of Medical Sciences, National Academy of Sciences-National Research Council.

OAK RIDGE INSTITUTE OF NUCLEAR STUDIES

The Special Training Division of the Oak Ridge Institute of Nuclear Studies has announced a partial schedule of courses to be offered during the next twelve months.

The Institute, a non-profit educational corporation of 32 southern universities, conducts four-week courses in the basic techniques of using radioisotopes in general research work, and special and advanced courses of varying duration which stress applications of radioisotopes in specific fields of scientific endeavor.

The 47th through the 53rd basic courses, which are limited to 32 participants, will be held on the following dates:

48th	January 9–February 3, 1956
49th	February 6–March 2
50th	April 16–May 11
51st	June 4–29
52nd	July 16–August 10
53rd	August 13–September 7

The Institute's basic courses are designed to assist mature scientific and technical personnel in obtaining in a short time sufficient facility in the use of radioisotopes to utilize them safely and efficiently in their own research work. Minimum scholastic requirement for enrollment is a bachelor's degree, preferably in a scientific field, although no specific courses are required as prerequisites. Tuition for the basic course is $25.00.

Application blanks and further information may be obtained by writing Dr. Ralph T. Overman, chairman, Special Training Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tennessee. Applications and supporting letters should be in the hands of the Institute three months in advance of the starting date of the course for which application is made.

UNIVERSITY OF CHICAGO ADDS NEW PHYSICS COURSES

The University of Chicago has approved two new courses leading to the M.S. degree in Radiological Physics or in Health Physics. Both degrees are awarded by the Department of Radiology, and students will be accepted in the Fall Quarter, 1955. These courses are designed to give the student such academic background and practical understanding of the problems encountered as will enable him to take his place immediately in these two rapidly growing fields. Students entering these courses should have completed the equivalent of the University of Chicago B.S. degree in Physics—but must, in any case, complete all of those requirements for the Master's degree. Two years' residence is required because of the broad scope of the academic program, the second year of which is spent one-half time in academic work and one-half time in service in the department at a nominal rate of pay. Seventeen quarters course work give the student a strong background in Physiology, Biochemistry, Biophysics, Anatomy, Toxicology, and Radiological Physics. Additional information may be obtained by addressing Lester S. Skaggs, Department of Radiology, The University of Chicago, 950 East 59th Street, Chicago 37, Illinois.

AWARDS IN RADIOLOGICAL RESEARCH OF THE JAMES PICKER FOUNDATION

On behalf of the James Picker Foundation, the National Academy of Sciences-National Research Council announces the continued availability of funds in support of radiological research. Applications are reviewed by the Committee on Radiology of the Academy-Research Council's Division of Medical Sciences. Final determination of awards is made

by the Foundation upon recommendation of the Committee. The interests of the Foundation are oriented toward, but not necessarily limited to, the diagnostic aspects of radiology. Awards are not restricted to citizens of the United States. Applications for the fiscal year 1956–1957 must be submitted on or before December 1, 1955.

Grants-in-aid are designed to encourage research offering promise of improvement in radiological methods of diagnosis or treatment of disease.

Grants for Scholars are a transitional form of support, designed to bridge the gap between the completion of fellowship training and the period when the young scientist has thoroughly demonstrated his competence as an independent investigator. A grant of $6,000 per year will be made directly to the Scholar's institution as a contribution toward his support, or his research, or both. Initial grants are limited to one year, but renewal may be recommended. Applications should be submitted by the institution on behalf of the candidate.

Fellowships in Radiological Research, available under the program of the Foundation, are being announced separately.

Further details and application blanks may be obtained from the Division of Medical Sciences, National Academy of Sciences-National Research Council, 2101 Constitution Ave., N. W., Washington 25, D. C.

CONFERENCE ON ELECTRICAL TECHNIQUES IN MEDICINE AND BIOLOGY

The Eighth Annual Conference on Electrical Techniques in Medicine and Biology will be held November 14, 15, and 16 at the Shoreham Hotel in Washington, D. C. Sponsored by the American Institute of Electrical Engineers, the Institute of Radio Engineers and the Instrument Society of America, the Conference aims to promote understanding and cooperation among physicians, physiologists, biophysicists and engineers.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

Die Teleröntgentherapie. Von Prof. Dr. W. Teschendorf, Köln. Paper. Price, DM 8.70. Pp. 72, with 8 illustrations. Georg Thieme, Herdweg 63, Stuttgart, Germany, 1953.

In this monograph on teleroentgen therapy, Dr. Teschendorf describes three principal means of applying this type of therapy: (1) treatment of the entire body at each session, (2) treatment of the trunk partitioned into four sections, with the exception of the head and the extremities, and (3) treatment of particular sections of the body, such as metastatically involved areas, with a long focal skin distance and with small doses.

He feels that whole body irradiation is indicated primarily in the leukemias. Radiophosphorus is the treatment of choice in polycythemia vera in his opinion. Roentgen therapy is generally preferable to isotope therapy because it can be more carefully controlled in that it may be discontinued should the blood count drop too low or too fast. With P^{32} isotope therapy the dose, once given, is irretractable. The author specifies a platelet count of 100,000 and a white blood count of 2,000 as minimal requirements for generalized irradiation. The prothrombin value should remain constant during treatment.

Dr. Teschendorf administers 3–5 r every three or four days to leukemic patients. The ventral and dorsal surfaces of the body are exposed equally, protecting the genitalia and eyes. The minimum white blood count to be realized from the treatment is 20,000. The general condition of the patient and his ability to carry on his usual occupation are the criteria upon which the treatment is based.

Generalized irradiation is used in treating malignant lymphogranulomatosis only in those cases which exhibit an elevated sedimentation rate in the absence of peripheral adenopathy.

A curious observation is recorded by the author as regards Sternberg's disease. This condition is less rapidly progressive in women than in men. He therefore suggests the trial administration of female hormones concomitantly with roentgen therapy.

In generalized carcinomatosis, the authors have given 25–50 r per treatment to body sections of 40–60 cm. length, giving five treatments in one week to a total of thirty treatments with the higher dose and to a total of fifty treatments with the lower dose. There was no skin irritation but pigmentation was observed.

Generalized experimental irradiation of patients with pneumonias and pulmonary tuberculosis with doses of 3 r per week have produced apparent stimulation of the reticuloendothelial system with improvement of the patients' general condition.

This small book is clearly written and records useful data relative to sectional and whole body treatment with low intensity irradiation.

Kenneth L. Krabbenhoft, M.D.

An Atlas of Skull Roentgenograms. By Bernard S. Epstein, M.D., Associate Radiologist, The Jewish Hospital of Brooklyn, Brooklyn, New York; and Leo M. Davidoff, M.D., Neurosurgeron to the Mount Sinai Hospital, New York City, and Director of Neurological Surgery, the Beth Israel Hospital, New York City. Cloth. Price, $15.00. Pp. 415, with 603 illustrations on 315 engravings. Lea & Febiger, Washington Square, Philadelphia, 1953.

This book is a compendium of film reproductions illustrating the radiology of the skull. In this work, the authors have placed important emphasis on the plain roentgenogram, it being their belief that pneumoencephalography and cerebral angiography have been adequately handled elsewhere and that many important diagnostic features can be revealed by simple techniques.

The book is divided into several chapters including: (a) the normal skull, (b) congenital variations, anomalies and malformations, (c) traumatic changes, (d) infections, (e) brain tumors (general), (f) gliomas, primary sarcomas, and lipomas of the brain, (g) craniopharyngiomas and pituitary adenomas, (h) miscellaneous tumors, (i) tumors of the vault

of the skull, and (j) non-neoplastic diseases of the skull.

The book is an excellent one in every detail and reflects the broad experience of the authors in the field of radiology with which they have been identified for many, many years. Since emphasis has been placed upon pictorial presentation, the greater portion of the book is devoted to the reproduction of roentgenograms covering a wide range of pathology. In addition, however, there is considerable textual material that, even though it is proportionately small, contains more instructional content than many textbooks which are devoted specifically to the didactic aspects of skull radiology. The book is a "must" for all students of radiology.

Russell H. Morgan, M.D.

Craniography. Roentgenological Examinations without and with Contrast Mediums. By Prof. Mario Lenzi. Direttore dell' Istituto di Radiologia della Università di Modena. Price, L. 2,000. Paper. Pp. 77, with 38 illustrations. Casa Editrice Cappelli, Bologna, Italia, 1952.

Prof. Lenzi regards the craniographic examination as a precision examination, demanding clinical investigative ingenuity on the part of the radiologist as well as good technical methods. It is only in this way that the most valuable contributions can be made in support of the neurologist and neurosurgeon.

The first section of this paper bound atlas deals with normal craniological points and planes of reference as well as technical details of examination procedure. The author next describes investigative methods not employing contrast media.

Fractionated cisternography, encephalography, ventriculography and arteriography are presented as far as the standard positions and moments of filling are concerned. These serve as a basis for evaluating the many normal variations to be encountered.

The author has thoughtfully written this book with an Italian and an English text which appear side by side. It will surely be more widely useful as a result. This volume is particularly well illustrated and will be of value to the radiologist performing neuroradiological procedures.

Kenneth L. Krabbenhoft, M.D.

Physiology of the Eye; Clinical Application. By Francis Heed Adler, M.A., M.D., F.A.C.S., Professor of Ophthalmology, School of Medicine, University of Pennsylvania, and Consulting Surgeon, Wills Hospital, Philadelphia. Second edition. Cloth. Price, $13.00. Pp. 734, with 329 illustrations. C. V. Mosby Company, 3207 Washington Boulevard, St. Louis 3, Missouri, 1953.

This is a presentation of the recent findings of physiology of the eye gleaned from the experimental laboratory with the correlation, when possible, to clinical concepts. Great progress has been made in fields such as the dynamics of aqueous humor formation, the photochemistry of the retina, and the application of electrophysiologic techniques to retinal function. Basic considerations of ocular physiology such as the formation and elimination of the aqueous humor, the permeability characteristics of the cornea, and the hemodynamics of the ocular circulation are presented. The neuromuscular mechanisms which normally maintain the two eyes in alignment are described to provide a better medical and surgical approach to strabismus.

The first ten chapters are arranged topographically, discussing chapter by chapter the normal and deranged physiology in each part of the visual system. The remaining twelve chapters are concerned with general visual subjects such as light, the photochemistry of vision, electrical phenomenon, visual acuity, and color vision.

This second edition, appearing only three years after the first, includes much new material in the sections on the cornea, aqueous humor and vitreous which re-establishes its position to an even greater extent as the standard reference in this field.

Alston Callahan, M.D.

Fundamentals of Clinical Cancer. By Leonard B. Goldman, M.D. Clinical Professor of Radiotherapy, New York Medical College, Flower and Fifth Avenue Hospitals; Chairman, Tumor Conference and Director, Radiation Therapy Department, Queens General Hospital; Consultant Radiation Therapist, Flushing, Rockaway Beach and Triboro Hospitals, New York City. Cloth. Price, $8.75. Pp. 312, with 221 illustrations. Grune & Stratton, Inc., 381 Fourth Avenue, New York 16, New York, 1953.

The author's intent in producing this book has been to fulfill the need for such a reference for the management of early malignant lesions. There is plentiful literature on advanced malignancy but the early detection and subsequent early treatment of neoplastic diseases is not always adequately described. In general, the recommendations for treatment are concerned with "what to do" rather than "how to do."

Chemotherapy is discussed as a probable treatment of greater scope in the future and is limited in this text to those substances of definite proved value.

Biopsy methods of various types are described and the situations in which each is applicable are outlined. Particularly in reference to sarcomatous lesions of the soft tissues, it is wisely pointed out that "a biopsy specimen from a non-ulcerated tumor should be obtained by aspiration."

The general methods of treating malignant diseases are described briefly, including surgical, radiotherapeutic, chemotherapeutic, and hormonal means.

The prognostic figures for carcinoma of the larynx, as given by the author are somewhat misleading in that only laryngofissure is credited with a high (90–95 per cent) percentage of permanent five year results. It should be pointed out that properly administered roentgen therapy can produce similar results in 80–90 per cent of cases with lesions of the true cords.

A treatment which the reviewer would include in the management of carcinoma of the penis is the radium mold. Certainly surgical extirpation is the treatment of choice, but a large number of patients afflicted with this lesion refuse operation and then the next best treatment is thought to be that with a radium mold.

It is stated that Stage II carcinoma of the cervix uteri may be treated with radium or radical hysterectomy followed by external irradiation. In the opinion of the reviewer, there are few clinics which now regard hysterectomy as having any place in the management of cervical cancer except in the Stage I lesions. The author's recommendations for the treatment of other Stages of cervical carcinoma follow well accepted lines.

In regard to the treatment of leukemia, the author has a particularly sage statement, "The smallest amount of the least toxic treatment that relieves symptoms should be the guide in the treatment of leukemia."

The author is to be congratulated on an exceptionally well organized book. It is concisely written and would be an invaluable addition to the library of any physician who is occasioned to diagnose and treat cancer. It is clearly evident that the author has had extensive clinical experience in handling such problems. The book is admittedly dogmatic at times —a necessary characteristic of forceful writing and teaching.

Kenneth L. Krabbenhoft, M.D.

Planning Guide for Radiologic Installations. By The Committee on Planning of Radiologic Installations of the Commission on Public Relations of The American College of Radiology, Wendell G. Scott, M.D., Chairman. Cloth. Price $8.00. Pp. 336, with 72 illustrations, 54 tables and three appendices (30 illustrations and 39 tables). The Year Book Publishers, Inc., 200 E. Illinois Street, Chicago 11, Illinois, 1953.

With Dr. Scott in this important contribution to radiologic literature stand a host of eminent radiologists, physicists, architects, engineers and special consultants. These outstanding authorities have provided needed guidance in the field of radiologic planning. The first edition of the planning guide fills well current requirements for a pilot in the designing of radiologic facilities.

The text is thorough and well organized. Work flow charts are a most valuable inclusion in the book and they show how any activity may be analyzed to achieve maximal efficiency of operation. The importance of detailed planning is not only stressed but exemplified by the recommendations laid down in many chapters. The portion of a chapter dealing with installations for special diagnostic examinations, however, could be greatly expanded. Special diagnostic facilities easily could be made the subject of discussion in several additional chapters.

Protection is properly emphasized. Chapters dealing with radiation therapy and radioactive isotope areas, in particular, give specific references at points of discussion in the text. The numerous tables and graphs and the appendices, which consist of reprinted handbooks of the National Bureau of Standards, serve as ready references needed frequently in daily work. If

used only as a handy source of information and physical data, the book would be a serviceable addition to every radiologist's library.

The volume is an invaluable storehouse of recorded knowledge, much of which has been gained by the experience of many colleagues. While the suggestions laid down cannot be adapted with equal facility to all local situations, nevertheless, it is probable that had such a guide been available during the planning phase of many places of radiologic practice now in existence, a large number of inconveniences would have been avoided. The text should be a subject of exhaustive study by all radiologists who are advisors to, or participants in the development of, any new installation or the renovation of an old facility, whether it be large or small, hospital department or private office. It is strongly recommended that the book be given the close attention of hospital architects and commercial planning service engineers and it should be helpful to medical administrators.

The medical profession as a whole is indebted to the American College of Radiology for sponsoring the "Planning Guide for Radiologic Installations." The publication of other editions, as new developments in the field warrant, should be encouraged and actively supported by members of the specialty of radiology.

Ernest H. Wood, M.D.

A Handbook of Radiotherapy. By Walter M. Levitt, M.D., F.R.C.P. (Lond.), F.F.R., D.M.R.E. (Camb.) of Lincoln's Inn, Barrister-at-Law. Associate Physician to the Department of Radiotherapy, St. Bartholomew's Hospital, London; late Physician in Charge, Department of Radiotherapy, St. George's Hospital; late Examiner in Radiotherapy for the Fellowship, Faculty of Radiologists; and Lecturer in Radiotherapy for the D.M.R.E., Cambridge. Cloth. Price, $6.50. Pp. 232, with illustrations. Paul B. Hoeber, Inc., 49 East 33rd Street, New York 16, New York, 1953.

The author intended this book for the senior and post-graduate medical student up to the registrar standard and has admirably realized his aim. The first chapters are devoted to a discussion of fundamental physical concepts as they pertain to roentgen rays, radioisotopes, and radium, assuming that the reader has no previous knowledge of physics. Roentgen beam treatment planning, radioisotope and radium therapy are next described in moderate detail.

Radiobiological studies of both in vitro and in vivo nature are cited from the standpoint of the individual tissues. Constitutional and local effects of radiation exposure of acute and chronic types are also considered. The effects of time and intensity factors, as well as inherent cellular characteristics relating to tumor sensitivity, give a good basis for understanding the clinically applied radiotherapeutic techniques.

An important chapter is devoted to the general management of the patient before, during, and after radiotherapy. The problems of diet and sepsis are of primary importance in the pre-treatment period. During the administration of the therapy, constitutional effects and reactions in the skin, eye, and mucous membranes demand the most attention. After the treatment series is concluded, any chemical or physical irritation is to be avoided where the skin included in the treated areas is concerned.

Those chapters describing treatment techniques are well written and concisely present well established methods of managing malignant diseases. Where applicable, the nonmalignant conditions best treated by radiation therapy are discussed in their appropriate sections.

An appendix lists the staging of carcinomas of the breast and cervix commonly in use. A second appendix comprises an extract of the International Recommendations on Radiological Protection.

This handbook is of convenient size, well illustrated, and will aid the student in placing the many facets of radiation therapy in their proper perspective.

Kenneth L. Krabbenhoft, M.D.

Tumors of the Peripheral Nervous System. Atlas of Tumor Pathology. Section II—Fascicle 6. By Arthur Purdy Stout, M.D., Professor of Surgery, Columbia University, College of Physicians and Surgeons, New York City. Paper. Price, 60 cents. Pp. 57, with 56 illustrations. Published by the Armed Forces Institute of Pathology, under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D.C., 1949. For sale by the American Registry of Pathology, Armed Forces Institute of Pathology, Washington 25, D.C.

This fascicle deals with tumors of the peripheral nervous system and therefore lesions arising from the Schwann or sheath cells, the sympathetic ganglion cells, and the paraganglionic cells. They are relatively few in number but display great variation in their appearance and behavior.

The term "malignant Schwannoma" is preferred to "neurogenic sarcoma" because of the uncertainty of malignant fibrous tumors arising from mesodermal elements of the nerve sheath. Tumors with their origins in heterotopic central nervous system tissue are also discussed.

Photomicrographs of histologic tissue sections excellently illustrate the text.

KENNETH L. KRABBENHOFT, M.D.

TUMORS OF THE MEDIASTINUM. ATLAS OF TUMOR PATHOLOGY. Section V—Fascicle 18. By Hans George Schlumberger, M.D., Professor of Pathology, Ohio State University, College of Medicine, Columbus, Ohio. Paper. Price, 75 cents. Pp. 88, with 75 illustrations. Published by the Armed Forces Institute of Pathology, under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C., 1951. For sale by the American Registry of Pathology, Armed Forces Institute of Pathology, Washington, 25, D. C.

The most frequently encountered tumors in the anterior mediastinum are thymomas and teratomas; in the anterior and middle mediastinum, lymphoblastomas; and in the posterior mediastinum, tumors of the intercostal nerves, sympathetic nerve trunks, and ganglia.

Tumors of aberrant tissue forming adenomata of the thyroid and parathyroids may be found in the anterior mediastinum. Cystic lesions here arise from the thymus and from teratomata. Pericardial cysts are found in the anterior and middle regions, while bronchogenic cysts occur in the superior and middle divisions. Gastroenteric cysts are found in the posterior mediastinal compartment.

It is stated that the safety of exploratory thoracotomy now precludes the use of the roentgen therapeutic test dose. This statement may be contested in some situations.

Tumors of the thymus, esophagus, and cardiovascular system are not included in this fascicle. The illustrations are well integrated with the text.

KENNETH L. KRABBENHOFT, M.D.

TUMORS OF THE BREAST. ATLAS OF TUMOR PATHOLOGY. Section IX—Frscicle 34. By Fred W. Stewart, M.D., Pathologist to Memorial Hospital, Professor of Pathology, Cornell University Medical School, Attending Pathologist of New York Hospital, New York City. Paper. Price, $1.10. Pp. 114, with 68 illustrations. Published by the Armed Forces Institute of Pathology, under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D.C., 1950. For sale by the American Registry of Pathology, Armed Forces Institute of Pathology, Washington 25, D.C.

This fascicle deals only with primary malignant tumors of the breast arising from either parenchymatous or stromal components. No distinction is made between the male and female breast since the histological types of lesions involving them are the same. A single exception is the "lobular carcinoma" which the author has never seen in a male breast, "presumably because the male breast does not possess lobules."

Cancer may arise in any postpubertal breast; no well-substantiated example of perpubertal cancer of the adult type has been seen. The concept of precancerous breast lesions is discussed primarily as an overworked idea, the author suggesting that "the most frequent precancerous lesion of the breast is a cancer of the opposite breast."

A plea is made for keeping pathological classifications of breast lesions as simple as possible. For prognostic reasons, we should ask: (1) Is the tumor infiltrating? (2) Is it infiltrating diffusely or in a circumscribed manner? (3) Is there obvious lymphatic or venous invasion? and (4) Has it metastasized to the lymph nodes? If so, where are they located as to the base, mid-portion, and apex?

The photomicrographs and a few gross specimens reproduced in full color excellently illustrate the text.

KENNETH L. KRABBENHOFT, M.D.

BOOKS RECEIVED

PROGRESS IN BIOPHYSICS AND BIOPHYSICAL CHEMISTRY. Volume 3. Edited by J. A. V. Butler, Professor of Physical Chemistry, University of London, Chester Beatty Research Institute, Royal Cancer Hospital, London; and J. T. Randall, F R.S., Wheatstone Professor of Physics in the

University of London at King's College. Cloth. Price, $9.50. Pp. 386, with numerous illustrations. Academic Press Inc., 125 East 23rd Street, New York 10, New York, 1953.

Clinical Roentgenology. Volume II. The Head, Neck and Spinal Column. By Alfred A. de Lorimier, M.D., Radiologist, Saint Francis Memorial Hospital, San Francisco, California; Henry G. Moehring, M.D., Radiologist, Duluth Clinic, Duluth, Minnesota; John R. Hannan, M.D., Radiologist, Lake County Memorial Hospital, Painesville, Ohio. Cloth. Price, $18.50. Pp. 488, with 734 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1954.

Chronic Otitis. A Critical Analsyis. By Marcus Diamant, M.D., Head of the Ear, Nose and Throat Department, The Central County Hospital, Halmstad, Sweden. Paper. Price, Swiss francs 23.-. Pp. 190. S. Karger Ltd., Holbeinstrasse 22, Basel, Switzerland, 1952.

The Roentgenologist in Court. By Samuel Wright Donaldson, M.D., Roentgenologist, St. Joseph Mercy Hospital, Ann Arbor, Michigan. Second edition. Cloth. Price, $7.75. Pp. 358. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1954.

The Heart Beat; Graphic Methods in the Study of the Cardiac Patient. By Aldo A. Luisada, M.D., Associate Professor of Medicine and Director, Division of Cardiology, The Chicago Medical School, under a Teaching Grant of the National Heart Institute, U. S. Public Health Service; Associate Visiting Physician (Acad. Staff) and Chief of Cardiac Clinics, The Mount Sinai Hospital of Chicago; Chief of Service and Cardiologist, La Rabida Hospital for Rheumatic Children. Cloth. Price, $12.00. Pp. 527, with 311 illustrations. Paul B. Hoeber, Inc., 49 East 33rd Street, New York 16, New York, 1953.

A Manual of Tropical Medicine. By Thomas T. Mackie, M.D., Colonel, M.C., A.U.S. (Retired). Chairman, The American Foundation for Tropical Medicine; George W. Hunter, III, Ph.D., Colonel, M.S.C., U.S.A., Chief, Section of Parasitology-Entomology, Fourth Army Area Medical Laboratory, Brooke Army Medical Center, Fort Sam Houston, Texas; C. Brooke Worth, M.D., Field Staff Member, Division of Medicine and Public Health, The Rockefeller Foundation. Second edition. Cloth. Price, $12.00. Pp. 907, with 304 illustrations, 7 in color. W. B. Saunders Company, West Washington Square, Philadelphia 5, Pennsylvania, 1954.

Diagnosis and Localization of Brain Tumors: A Clinical and Experimental Study Employing Fluorescent and Radioactive Tracer Methods. By George E. Moore, M.D., Ph.D., Markle Scholar in Medical Science; Director, Roswell Park Memorial Institute. Cloth. Price, $10.50. Pp. 217, with 66 illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1953.

The Billroth I Gastric Resection; With Particular Reference to the Surgery of Peptic Ulcer. By Horace G. Moore, Jr., M.D., Wilmington, North Carolina; formerly Instructor in Surgery, University of Washington School of Medicine; formerly Chief Resident in Surgery, King County Hospital, Seattle; and Henry N. Harkins, M.D., Ph.D., F.A.C.S., Professor of Surgery and Executive Officer of the Department of Surgery, University of Washington School of Medicine; Surgeon-in-Chief, King County Hospital, Seattle; formerly Associate Professor of Surgery, Johns Hopkins University School of Medicine. Cloth, Price, $7.50. Pp. 175, with 36 figures and 18 tables. Little, Brown & Company, 34 Beacon Street, Boston 6, Massachusetts, 1954.

Tenth Annual Report to the Honourable the Minister for Health and Home Affairs. For the Year Ended 30th June, 1954. Presented to Parliament and Ordered to be Printed. Paper. Pp. 17, with numerous tables. A. H. Tucker, Government Printer, Brisbane, 1954.

Medizinische Röntgentechnik. Teil II. Physikalishtechnischer Teil. Edited by Prof. Dr. med. Herbert Schoen. Cloth. Price, DM 27.-. Pp. 360, with 217 illustrations. Georg Thieme, Herdweg 63, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

Tumors of the Soft Tissues. Atlas of Tumor Pathology. Section II—Fascicle 5. By Arthur Purdy Stout, M.D., Professor of Pathology, Columbia University, College of Physicians and Surgeons, New York City. Paper. Price, $2.00. Pp. 138, with 78 illustrations. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C., 1953. For sale by the American Registry of Pathology, Armed Forces Institute of Pathology, Washington 25, D. C.

Tumors of the Stomach. Atlas of Tumor Pathology. Section VI—Fascicle 21. By Arthur Purdy Stout, M.D., Professor of Pathology, Columbia University, College of Physicians and Surgeons, New York City. Paper. Price, $1.75. Pp. 104, with 66 illustrations. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C., 1953. For sale by the American Registry of Pathology, Armed Forces Institute of Pathology, Washington, D. C.

Cumulative Index to the First Fifteen Semiannual Reports to Congress. By United States Atomic Energy Commission. Paper. Price, $.35. Pp. 118. United States Government Printing Office, Washington, D. C., 1954.

Seventeenth Semiannual Report of The Atomic Energy Commission. By United States Atomic Energy Commission, Lewis L. Strauss, Chairman. Paper. Pp. 138, with tables. United States Government Printing Office, Washington, D. C., 1955.

Basic Curriculum and Teacher's Syllabus in X-Ray Technology. Paper. Price, $1.00 plus $.15 postage. Pp. 37. Published by The American Society of X-Ray Technicians and distributed through the Executive Secretary, Genevieve J. Eilert, 16 Fourteenth Street, Fond du Lac, Wisconsin, 1954.

Biological Effects of External X and Gamma Radiation. Part I. Edited by Raymond E. Zirkle, Professor of Radiobiology and Biophysics, University of Chicago; Consultant, Division of Biological and Medical Research, Argonne National Laboratory; formerly Principal Biologist, Manhattan Engineer District (Metallurgical Laboratory, University of Chicago, and Clinton Laboratories, Oak Ridge, Tennessee). First edition. Cloth. Price, $7.25. Pp. 530, with numerous illustrations and tables. McGraw-Hill Book Company, Inc., 330 West 42nd Street, New York 36, New York, 1954.

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

765 Wolf, Bernard S., Newman, Charles M., and Schlesinger, Benno. The diagnostic value of the deep cerebral veins in cerebral angiography. *Radiology*, Feb., 1955, *64*, 161–177.

765 Carotid angiography has become an established procedure, but most of the emphasis has been placed on changes in the arterial phases. The authors emphasize the importance of changes in the deep veins of the brain. The deep veins serve as extraordinarily useful landmarks for the adjacent cerebral structures, and it is pointed out that these veins are in a very constant location.

765 Excellent discussion and drawings of the anatomy of the deep venous circulation are presented. The authors show that before assigning undue significance to small changes in the venogram, the lateral projection must be true.

766 The roentgenographic changes noted on venograms of patients with various types of lesions are discussed, and it is noted that with central neoplasms, angiographic evidence may be confined to these vessels. Changes in the deep veins of the brain as a result of expanding intracranial lesions follow reasonable patterns based on anatomical features. Central neoplasms produce displacements in the nature of local distortion while peripheral neoplasms cause en bloc types of displacement.

766 Although many of the changes seen on the venogram can be diagnosed by simple inspection, it was felt that some means of measurement would be of great value. Three points (anterior, mid and posterior) on the internal cerebral vein were located and a transparent template was constructed which could be used to measure small amounts of displacement. Measurements were made from a base line extending from the tuberculum sellae to the lower margin of the sulcus for the transverse sinus.

767 Despite the fact that the internal cerebral vein is quite constant in position and that the template described has been reliable in locating it, it must be emphasized that the observations of changes in the venous phases must be consistent and correlated with the findings in the arterial and capillary phases as well as with the clinical features.—*A. Ralph Watson, M.D.*

767 Odén, Sven. Triurol in cerebral angiography. *Acta radiol.*, Feb., 1955, *43*, 97–103. (From: Roentgen Department of Serafimerlasarettet, Stockholm, Sweden.)

768 An ideal contrast medium for cerebral angiography requires that it should not entail any risk of complications at the time of examination nor any discomfort to the patient, should not cause late damage, and it should be rapidly and easily eliminated from the organism. Triurol is the trade name of a preparation manufactured in Sweden. In order to compare the qualities of triurol and umbradil, double examinations were carried out in 102 cases. As a rule, one contrast medium was injected into the internal or common carotid artery of one side and the other into the corresponding vessel on the other side. In these examinations 7 ml. were injected per injection and the number of injections per examination was never less than three and never higher than six. More than half of the patients considered the discomfort was considerably less with triurol 25 per cent than with umbradil 35 per cent, and the contrast density obtained with triurol was quite satisfactory. This material was almost completely lacking in the objective changes that contrast injections may cause such as flushing of the skin and none of the reactions were sufficiently severe to require more than local anesthesia for the procedure.

768 Following comparative experimental studies, triurol was adopted for routine use and subsequently 142 additional cases were examined using this material. One of these patients suffered rapidly transient urticaria but no other complications were observed. The employment of umbradil in cases of recent head injury has always meant a risk of possible serious deterioration in the condition of the patient in connection with contrast medium examination. Three such cases examined with triurol were not unfavorably affected by the examination.

768 In rapid serial angiography only 3 to 4 ml. of triurol per injection has been used and this produced excellent results without serious discomfort to the patient. On the basis of the experience of the author, it appears that the amount injected plays an important role in creating discomfort to the patient although undoubtedly osmotic pressure of the contrast medium is also a significant factor.—*Lois Cowan Collins, M.D.*

768 Kim, Sun Keun. Cerebral paragonimiasis; report of four cases. *J. Neurosurg.*, March, 1955, *12*, 89–94. (From: 3rd Army Hospital [Republic of Korea], Pusan, Korea.)

768 Paragonimiasis, or infection by the lung fluke, is known to be endemic in certain areas of the Far East, particularly in Korea, Japan and Formosa.

768 It is known that the *Paragonimus westermani* may involve the lungs, pleura, liver, intestinal wall, mesenteric lymph nodes, testes, muscles, peritoneum, and brain. Four cases of cerebral cysts caused by paragonimiasis which were encountered during the last year are reported because of the rarity of cerebral involvement.

768 Three of the 4 patients were infected before they were twelve years of age, 1 being thirty-two years old at the time of surgery. In 3 instances there were

epileptiform seizures as an early symptom. One patient had symptoms of increased intracranial pressure. All patients with symptoms of more than a year in duration had visual distrubances. Aphasia was noted to a degree in all patients and perhaps was related to involvement of the speech center. All patients were right-handed.

The cerebral cortex and subarachnoid space were the main areas affected. In all cases there was involvement of the frontal, temporal and parietal lobes and in Cases 2 and 3 the occipital lobe was also involved. None had apparent cerebellar lesions. All the cysts were thick-walled and they were calcified. The amount of calcification and the size of the cysts appeared to be related to the duration of symptoms. The perfectly encapsulated cysts were easily removed but several had areas of indistinct boundaries, which made their removal difficult.

All the 4 patients with symptoms of intracranial masses were found at surgery to have intracranial paragonimiasis. The diagnosis in 3 cases was suggested by skull films showing multiple calcified nodules. In 1 case pneumoencephalograms demonstrated the presence of a space-occupying mass. In 3 of the 4 cases it was impossible to remove all the masses visible in the skull films. Three of the patients appeared to be benefited by surgery.

The author believes that the frequency of intracranial paragonimiasis in the Far East, especially in Korea, is greater than had been thought. When these cysts produce symptoms of an intracranial mass, they should be removed surgically. It is pointed out that there were no good studies of the course of asymptomatic intracranial cysts caused by *Paragonimus westermani.*—*Robert D. Moreton, M.D.*

Jackson, Ira J., Earle, Kenneth, and Kuri, Jose. Solitary *Aspergillus* granuloma of the brain; report of 2 cases. *J. Neurosurg.*, Jan., 1955, *12*, 53–61. (From: Division of Neurological Surgery, Department of Surgery, and Department of Pathology, University of Texas and John Sealy Hospital, Galveston, Texas.)

Fungous infections of the central nervous system caused by Aspergillus are quite rare and the authors report 2 such cases of a solitary granulomatous mass in the brain. The infection usually involves the lungs, skin, external ears, paranasal sinuses and orbits and occasionally the bone and meninges.

Aspergillus is a microscopic fungus which is a regular inhabitant of the soil and occurs predominantly in warm damp climates. Review of the literature reveals that the central nervous system may be involved as part of a systemic infection with cerebral metastases or by direct extension from an adjacent portal of entry. The paranasal sinuses, nose, and orbits have been postulated as sites of entry.

The cases are presented and discussed in detail. Both had large granulomatous tumor masses in the frontal lobes. The authors note that special strains are needed to confirm the diagnosis and they believe that the pathologist must be aware of the possibility of a specific granuloma in order to avoid an erroneous diagnosis as was done in one of the cases presented—*Richard E. Kinzer, M.D.*

Neck and Chest

Donner, M., and Teschendorf, W. Zur Funktionsdiagnostik der Speiseröhre. (Functional diagnosis of esophageal lesions.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Feb., 1955, *82*, 202–208. (From: Strahleninstitut der Allgemeinen Ortskrankenkasse, Köln, Germany.)

The authors use gelatin capsules filled with barium to demonstrate levels of stenosis or spasms in the esophagus.

The capsules come in three sizes: 12 by 20 mm., 9 by 15 mm., and 4.5 by 7.5 mm. Since these capsules dissolve after a short time, they do not cause obstruction. They may be used to determine progress of lesions, to show increases or decreases in stenosis and they may be helpful in localizing lesions to be treated by radiation therapy. The capsules are arrested at the proximal end of organic lesions but are also often arrested at sites of spasm proximal to diverticula, ulcers, or other esophageal disturbances. However, the barium will flow distal to the capsule and any organic lesion distal to the level of the capsule may be studied without any interference.

The capsule technique has proved of value in the study of the enlarged left auricle in cases of mitral valvular disease, because the flow of barium is slower than without the use of the capsules.—*Joseph Zausner, M.D.*

Forshall, Isabella. The cardio-oesophageal syndrome in childhood. *Arch. Dis. Childhood*, Feb., 1955, *30*, 46–54. (From: Alder Hey Children's Hospital, Liverpool, England.)

The term "cardio-oesophageal syndrome" is used to cover all infants and children with incompetence of the cardia. A series of 93 cases was analyzed and for study purposes, these were divided into two groups, those in whom the cardia was above the diaphragm, or so-called sliding hernia, and those with lax esophagus with the cardia below the diaphragm. The course of the disease, prognosis, and probable etiology are different in these two groups.

In the first group, the lax esophagus with the cardia below the diaphragm, there were 58 cases, or 69 per cent of the entire series studies. This condition probably has a nervous or a neurogenic basis which involves the lower two-thirds of esophagus, the cardia, and perhaps occasionally the gastroin-

testinal tract below the cardia. The condition is self-limiting and at least three quarters of these children will recover with simple treatment, though serious complications are common. It is usually amenable to medical care consisting principally of keeping the baby upright during the act of feeding. Occasionally, surgery consisting of narrowing of the hiatus, is indicated. Four children of this group developed esophagitis with resultant shortening of esophagus and pulling of the cardia up into the thorax. One developed a chronic esophageal ulcer with stricture.

The group in which the cardia was above the diaphragm, or sliding hernia group, consisted of 35 cases. The author feels that the migration of the cardia into the thorax is probably dependent upon the difference in the thoracic and intra-abdominal pressure, and that a poorly developed hiatus bears a heavy responsibility and is the congenital element in this type of hernia. Esophagitis is almost invariably seen in this group. Hematemesis occurred in about 51 per cent of the cases, whereas it was present in only about 26 per cent of the lax esophagus group. These babies show the same tendency to contract chest infections, gestroenteritis, and to aspirate vomitus as the lax esophagus cases. The following complications were observed: (1) shortened esophagus, (2) peptic ulcers, (3) stricture. In this group operation is usually necessary, and 30 of the 35 patients were treated surgically. A thoracic approach to the esophagus and a transdiaphragmatic approach to the stomach proved most satisfactory and no recurrence occurred in 27 cases so treated. Nine cases were treated medically, but of these, 4 responded unsatisfactorily and required surgery later. Two patients treated medically died, one of pneumonia at the age of one month and one of aspiration of vomitus and hematemesis at the age of three months.

There is evidence to believe that lax esophagus and sliding hiatal hernia are etiologically distinct conditions. They are both serious problems because of the high incidence of complications. Although the lax esophagus will usually respond to medical treatment, the sliding hiatal hernia will almost always require surgical intervention.—*Lois Cowan Collins, M.D.*

Ritter, J. Sydney. Aortography. *J. Urol.*, Jan., 1955, *73*, 155–161. (Address: 755 Park Ave., New York 21, N. Y.)

Aortography is of inestimable value in the diagnosis of renal lesions. The indications for aortography should be definite and in no instance should the procedure be carried out unless its use is justifiable.

The author recommends the use of 80 per cent sodium iodide warmed to a temperature of 37 degrees, a 17 or 18 gauge needle about 8 inches long and a Luer-Lok 20 cc. syringe of normal caliber. Nervous or high strung individuals may receive a short pentothal sodium general anesthesia at the time of injection.

Indications for aortography include differentiation of renal neoplasms, cysts, congenital aplasia or hypoplasia, renal ptosis, pyelonephritis and lesions of the arterial renal vessels. Six illustrations are presented to show examples of these indications.

In the author's series complications have not been a serious factor.—*George W. Chamberlin, M.D.*

Eldridge, Frederic L., Hultgren, Herbert N., Liu, Chi Kong, and Blumenfeld, Margaret. A study of the clinical reactions to venous angiocardiography. *New England J. Med.*, Feb. 17, 1955, *252*, 259–263. (From: Department of Medicine, Stanford University School of Medicine, San Francisco, Calif.)

The clinical reactions to venous angiocardiography among 120 patients are analyzed. Seventy-seven patients were cyanotic and 43 were acyanotic. Fifty-two patients received 70 per cent diodrast, 44 received 75 per cent neo-iopax and 24 received 70 per cent urokon sodium. Respectively, 38, 32 and 15 were ten years of age or less.

Severe reactions (apnea, laryngeal spasm, Cheyne-Stokes respiration, cardiac arrhythmias, shock, pulmonary edema, convulsion, syncope and prolonged mental confusion) were more common when diodrast and neo-iopax were used then when urokon was used, and tended to appear in increasing numbers when higher doses of the agent were administered (in terms of body weight), when cyanosis was present and when patients were younger. Urokon did not cause these severe reactions, even after two injections, and the latitude as to size of the dose was much greater when urokon 70 per cent was used.

It is noted, however, that one death in this group occurred when urokon was administered to a child thirteen weeks old. In their total series, in which 300 angiocardiograms were made, there were 6 deaths: 3 followed the use of urokon, 2 occurred after the use of diodrast and 1 took place after neo-iopax had been administered. Five of the 6 who died were children with congenital heart disease (4 were cyanotic); and 1 had bronchogenic carcinoma.

The authors believe that the toxic effects of the agents were primarily responsible for the deaths. Although they feel that urokon is associated with a lower incidence of severe reactions, the 3 deaths recorded after it was injected force one to reserve judgment on this substance.—*André J. Bruwer, M.B.*

Corday, Eliot, and Elkin, Milton. Visualization of caudal surface of heart by use of carbonated beverage. *J.A.M.A.*, Feb. 26, 1955, *157*, 712–713. (Address: Dr. Corday, 436 N. Roxbury, New York, N. Y.).

Roentgenologic demonstration of downward enlargement of the left ventricle is difficult, due to the subdiaphragmatic increase in density caused chiefly by the stomach. Seven ounces of a commercial carbonated beverage, such as soda water or ginger ale, was given to patients just prior to the roentgenologic examination. A larger stomach bubble was produced through which the left lower border of the heart was visible. Cardiac measurements can be made more accurately by this method, and it was found that as much as one-third of the anterior surface of the heart may be invisible on routine chest roentgenograms. Fluoroscopic study of the heart is also enhanced and intracardiac and pericardial calcifications are better shown. The authors demonstrated a left ventricular aneurysm that was not visible on routine fluoroscopic study.

Nearly all of the cases showing downward enlargement of the left ventricle were of arteriosclerotic or hypertensive type. Rheumatic valvular disease rarely caused downward enlargement of the left ventricle.—*Charles W. Cooley, M.D.*

McKusick, Victor A., and Cooley, Robert N. Drainage of right pulmonary vein into inferior vena cava; report of a case, with a radiologic analysis of the principal types of anomalous venous return from, the lung. *New England J. Med.*, Feb. 24, 1955, *252*, 291–301. (From: Departments of Medicine and Radiology, Johns Hopkins University School of Medicine and Hospital, Baltimore, Md.)

This is a review of 20 cases of anomalous return of part or all of the pulmonary venous blood.

Two conditions which are readily recognized in routine roentgenograms of the thorax are: (1) drainage of the right lung to the inferior vena cava via a large paracardiac vein, and (2) total anomalous drainage of both lungs via a persistent left superior vena cava, which in turn drains into the right atrium. In the patients who survive, an atrial septal defect has to be present.

Several other types of anomalous venous return are described. For a diagnosis of most of them, angiocardiography is an essential procedure.

A summary of the findings would be impractical, and the illustrations in the original article should be consulted.—*André J. Bruwer, M.B.*

Billings, F. T., Jr., and Couch, O. A., Jr. Pericardial calcification and histoplasmin sensitivity. *Ann. Int. Med.*, March, 1955, *42*, 654–658. (From: Department of Medicine, Vanderbilt University Medical School, Nashville, Tenn.)

The cause of calcification of the pericardium in many instances is obscure. Although frequently it is due to tuberculous infection, pneumococcus, and other purulent bacterial infections, rheumatic fever and trauma, many times the etiology remains unknown.

The authors present 2 cases of young adults who, on chest roentgenograms, showed a thin curvilinear shell of calcium in the pericardium at the left cardiophrenic angle. First and second strength tuberculin intradermal sensitivities were negative. Both had strongly positive reactions to histoplasmin, 0.1 mg. injected intradermally. This may or may not have been related to the pericardial calcification. Histoplasmosis is suggested chiefly to stimulate further interest in this disease as another cause of calcified pericardium and perhaps even of constrictive pericarditis.—*William C. MacCarty, Jr., M.D.*

Gough, J. Correlation of radiological and pathological changes in some diseases of the lung. *Lancet*, Jan. 22, 1955, *1*, 161–162. (From: Department of Pathology, Welsh National School of Medicine, Cardiff, Wales.)

For several years the author has been using paper-mounted sections of whole lungs or lobes in comparing morbid anatomical changes with the roentgenological changes found during life. The sections are thin enough to be suitable for microscopy, are mounted on paper rather than glass and certain glycol derivatives are used to preserve the natural colors. Staining is thus unnecessary, except for special purposes such as demonstration of hemosiderin by the prussian-blue technique.

While the author's primary object is the study of pneumoconiosis in coal miners' lungs, he discusses in this article mitral stenosis, microlithiasis alveolaris pulmonum, emphysema and uremic edema. The paper-mounted sections are easy to handle, do not deteriorate and can be filed with the corresponding roentgenograms.

In mitral stenosis the distribution of hemosiderin pigment producing the punctate roentgenological shadows is well shown. More dense and larger opacities particularly in the lower lung fields were found to be areas of ossification. Horizontal thin linear markings in the lower lung fields were not areas of linear atelectasis but were found by Fleischner on the paper-mounted sections to be due to deposits of hemosiderin in the septa between the secondary lobules. In most lungs hemosiderin is deposited in foci in the center of the lobules, but in some it is mainly in the septa. Not all the lines seen in mitral stenosis were due to hemosiderin. Some were due to edema of the connective tissues of the septa with distention of the lymphatics. This type of line may be present during periods of cardiac failure, disappearing when the edema subsides.

Microlithiasis alveolaris pulmonum is a rare condition producing an intense radiopacity of the lungs due to development of calcospherites and bone in

the lung. It is often labelled chronic hemosiderosis or severe ossification in tuberclulosis.

Roentgenographically, the degree and type of emphysema is very difficult to assess. The emphysema in patients with chronic bronchitis and in status asthmaticus appears much the same. Anatomically in status asthmaticus there is simple overdistention of lung without breakdown of lung tissue to form bullae. In chronic bronchitis and bronchiectasis bullous emphysema due to destruction of lung tissue is common and such emphysema seems to be permanent.

The central edema of the lungs occurring in uremia is shown clearly in paper-mounted large sections. The conception of the lung anatomy is that each lobe is divisible into a lobar root, a medulla and a cortex. The edema in this condition is limited to the medullary part.—*Arthur B. Smith, M. D.*

Warner, A. L., Palladino, N. M., Schwartz, W., and Schuster, A. The relationship of agenesis of the lung to emphysema and cor pulmonale. *J. Pediat.*, Feb., 1955, *46*, 200–209. (Address: Dr. Palladino, 2 Rural Gate, Plainview, L. I., N. Y.)

By bronchoscopy, bronchography and angiocardiography an eight year old Negro boy was proved to have complete absence of the left lung including bronchi and pulmonary arteries. Pulmonary function studies failed to reveal any clear-cut abnormality. Except for intercurrent asthma, the patient was asymptomatic.

A review of the literature reveals a need for more physiologic studies in patients with this anomaly but in general, if they have no other congenital abnormality incompatible with life, they survive infancy and most of them are asymptomatic.—*H. G. Peterson, Jr., M.D.*

Lunseth, John H., Kirmse, Thomas W., Prezyna, Anthony P., and Gerth, Robert E. Insterstitial plasma cell pneumonia. *J. Pediat.*, Feb., 1955, *46*, 137–145. (From: Departments of Pediatrics and Pathology, Milwaukee County General Hospital, Milwaukee, Wis.)

A case is recorded of what is thought to be the first instance of interstitial plasma cell pneumonia reported from the United States.

This disease has been recognized with increasing frequency as a clinical entity in Switzerland and Scandinavia during the past ten years. Clinically, it is found in premature and debilitated full-term infants, has its apparent onset during the second to fifth months of life and manifests itself chiefly by severe tachypnea, dyspnea, cough and cyanosis. Anorexia and failure to gain ensue. Fever is usually absent unless there is secondary infection. The disparity between the severity of the respiratory distress and the lack of physical signs is impressive. Pulmonary roentgenograms show a diffuse, ground-glass cloudiness with scattered small focal areas of emphysema and focal confluent densities. Pneumothorax may be a complication. Treatment is largely symptomatic and supportive. The disease usually lasts for one or two months. The prognosis is poor and sudden, unexpected death occurs frequently. The mortality is variously reported as 15 per cent to 100 per cent with 50 per cent being about the average. The highest mortality rate is observed in premature infants. The principal pathologic feature is the encroachment on the air-exchange spaces of the lungs by an interstitial proliferation of mononuclear inflammatory cells, chiefly plasma cells, in an increased amount of reticulum. Some have reported hyaline-like membranes about the walls of alveolar ducts. In the case described, a hyaline layer in the lining of alveolar ducts was interpreted as a proliferation of smooth muscle on the basis of staining reactions.

The disease remains idiopathic though it has an epidemic pattern of spread and a similar type of pneumonitis has been produced in guinea pigs following injection of blood and secretions from patients. It is suggested that it may be a virus disease.—*H. G. Peterson, Jr., M.D.*

Adler, Richard H., Mantz, Frank E., Jr., and Ware, Paul F. The middle lobe syndrome and its relationship to certain aspects of middle lobe disease. *J. Thoracic Surg.*, March, 1955, *29*, 283–295. (From: Research and Development Branch, Laboratory Service and Surgical Service, Fitzsimons Army Hospital, Denver, Colo.)

The authors reviewed the problem of the middle lobe syndrome and believe that the term middle lobe syndrome and its relationship to certain conditions affecting the middle lobe have been used somewhat ambiguously. They contend that the diagnosis of middle lobe syndrome should not be made unless the following criteria have been met satisfactorily: (1) hilar or peribronchial lymphadenopathy, (2) bronchostenosis and (3) variable changes in the distal parenchyma, *i.e.*, atelectasis, bronchiectasis, chronic pneumonitis, fibrosis and even lung abscess, empyema and bronchopleural fistula.

The patient may present with cough, sputum, hemoptysis or a history of recurring pneumonia. He may be asymptomatic. The clinical diagnosis of middle lobe syndrome may distract the clinician from the many possible basic etiological agents of the condition. In children, tuberculous hilar lymphadenopathy is often responsible. While carcinoma of the middle lobe bronchus is said to be uncommon, it is a definite possibility in the older age groups. In many cases, only a nonspecific inflammatory

process will be found. Unusual causes are sarcoidosis and histoplasmosis. The authors present one case of each of the latter conditions—*Paul C. Olfelt, M.D.*

McBurney, Robert P., Memphis, Tenn., Jamplis, Robert W., Palo Alto, Calif., and Hedberg, Gustaf, Nopeming, Minn. Oil granuloma and lipoid pneumonitis: A complication of oleothorax; report of seven cases. *J. Thoracic Surg.*, March, 1955, *29*, 271–276. (Address: Dr. McBurney, Sanders Clinic, Memphis, Tenn.)

While the use of mineral oil or paraffin as a method of plombage in the chest cavity is decreasing because of other more satisfactory methods of treating tuberculosis, the idea that the use of oil as a plomb is without untoward effects persists.

Of the 76 cases at Nopeming Sanatorium, Nopeming, Minnesota in which mineral oil was used either intra- or extrapleurally, 7 (approx. 10 per cent) had complications in the form of either a pleurocutaneous fistula, chest wall granuloma, or oil pneumonitis due to aspiration following bronchopleural fistula. These 7 cases are described in detail.—*Paul C. Olfelt M.D.*

Tapiovaara, Juha. The pneumomediastinum. *Acta radiol.*, Feb., 1955, *43*, 104–112. (From: Roentgen Department, First Surgical University Clinic, Helsinki, Finland.)

A combined study by laminagraphy and pneumomediastinum is presented. The presacral injection of oxygen used for it offers simultaneous visualization of both the anterior and posterior mediastinum which is not obtained by the direct methods.

The author feels that this method shows great promise in helping differentiate the origin of mediastinal tumors. The air was found to outline the free borders of the tumors and demonstrate their sites of attachment.—*George A. Miller, M.D.*

Donegan, Charles K., and Nouse, Don C. Diagnostic difficulties in evaluating pulsating mediastinal masses. *J.A.M.A.*, March 5, 1955, *157*, 798–801. (Address: Dr. Nouse, 1915 Parkwood Ave., Toledo, Ohio.)

Four cases illustrating the problems of diagnosis of pulsating mediastinal tumors are presented.

This series points out clearly the limitation of the criterion used for differentiating between an arterial vascular lesion and a tumor; *i.e.*, that the former pulsates and the latter does not. The authors show that tumors with close proximity to the larger arteries pulsate and that arterial anomalous shadows may not pulsate vigorously. They feel that critical flouroscopic interpretation and roentgenographic studies by experienced observers continue to be the most important diagnostic procedures besides angiocardiography. In mediastinal tumors, angiocardiography usually reveals an essentially normal vascular arrangment and, therefore, diagnosis of vascular and extravascular lesions is easily established.

It is of interest that all of the tumors presented in this series were cystic in nature.—*P. B. Parsons, M.D.*

Abdomen

Joske, R. A. Pancreatitis following pregnancy. *Brit. M. J.*, Jan. 15, 1955, *1*, 124–128.

The relationship between pregnancy and pancreatitis has received relatively little attention in the literature but postpartum pancreatitis forms a distinctive syndrome.

Six cases are reported with symptoms beginning two weeks to nine months after delivery, the symptoms consisting of abdominal pain, vomiting and jaundice. Cholecystography is useful in establishing the diagnosis of associated cholelithiasis, which was present in 4 of the 5 cases investigated for this condition.—*Leslie K. Sycamore, M.D.*

Cocchi, Umberto. Hiatushernie, Hiatusinsuffizienz und Kardiainsuffizienz. (Hiatus hernia, hiatus insufficiency, and cardia insufficiency.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Feb., 1955, *82*, 184–195. (Address: 62 Scheideggstr., Zürich 2, Switzerland.)

Since the symptomatology of hiatus hernia and hiatus insufficiency is almost identical, a definitive diagnosis can be established only after thorough fluoroscopic examination in all available positions with the patient erect, supine, and prone as well as in both obliques for each position.

Careful observation will show that in the presence of hiatus hernia, the herniated portion of the stomach fills in retrograde manner after the stomach itself is filled with the contrast medium. In cases of insufficiency, the distal end of the esophagus becomes dilated and filled from above either immediately after swallowing the barium or after regurgitation of the meal through the insufficient cardio-esophageal sphincter. Hiatus insufficiency often leads to hiatus hernia but each condition may exist without the other.—*Joseph Zausner, M.D.*

Hilscher, W. M. Neue Gesichtspunkte zur Frage der Hiatushernien. Die ösophageale und paragastrale Hernie. (New observations in hiatus hernia. Esophageal and paragastric hernias.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Feb., 1955, *82*, 195–202. (From: Röntgenabteilung der Chir. Univ.-Klinik, Kiel, Germany.)

The author adds two new types to the classification of hiatus hernias; in both cases, the herniated site was beneath the diaphragmatic dome.

One patient had a normally long esophagus with its distal end invaginated into the gastric fundus simulating a para-esophageal hernia. Another patient had a dilated esophagus with a prolapse of its distal end below the diaphragm and adjacent to the stomach. These observations are important in selecting the proper surgical approach, since in subdiaphragmatic hernias the abdominal approach is much simpler.—*Joseph Zausner, M.D.*

Kantor, Herbert G., Evans, John A., and Glenn, Frank. Cholangiography; a critical analysis. *A.M.A. Arch. Surg.*, Feb., 1955, *70*, 237–252. (Address: Dr. Kantor, 525 E. 68th St., New York, N. Y.)

The authors present their analysis of 158 cases in which there were 171 operative and 234 postoperative cholangiograms. Stones were present in 40 cases, tumor in 8 cases, stricture in 6 cases and choledochal cyst in one. Of the 116 cases in which biliary duct pathology was present, the abnormality was demonstrated in 47.4 per cent by cholangiography.

The normal anatomy of the biliary tree is reviewed including measurements and anatomic variations. Description of the abnormal findings includes that of stones, air bubbles, spasm, stricture and tumor.

Criteria for adequate cholangiograms are set forth. Lack of filling of the hepatic ducts was responsible for 50 per cent of the unsatisfactory cholangiograms, with lack of visualization of the transduodenal portion second in importance. Details of technique are presented, which include the surgical aspects of operative cholangiography and recommended roentgenographic factors.—*Thomas F. Meaney, M.D.*

Cohn, Edwin M., Orloff, Theodore L., Sklaroff, David M., and Gershon-Cohen, Jacob. Philadelphia, Pennsylvania. The use of cholografin in the post-cholecystectomy syndrome. *Ann. Int. Med.*, Jan., 1955, *42*, 59–68.

The authors describe the postcholecystectomy syndrome as a group of symptoms for which cholecystectomy is performed with expectation of a cure which remains unchanged after operation. They point out that investigation of this syndrome has recently been made easier by the introduction of a new intravenously administered radiopaque medium known as cholografin. A brief history of the development of this medium is given and the technique and results of its use are reviewed.

In discussing the postcholecystectomy syndrome, the authors point out that one of the more common causes for a persistence of preoperative symptoms is found in erroneous diagnosis made prior to surgery. Missed common duct stones, enlarged cystic duct stump and spasm of the sphincter of Oddi are all mentioned as prime causes of the postcholecystectomy syndrome. The effect of morphine and of nitroglycerin on the sphincter of Oddi was demonstrated on 2 of the authors' patients during intravenous cholangiography. They note with interest that one of the patients complained of sudden onset of pain which was referred from the right upper quadrant of the abdomen through to the back at the same time that the common bile duct was observed to be enlarging. Distention of the common duct and increase in the opacification are both altered by the administration of nitroglycerin, at which time the opaque medium was seen to flow into the duodenum. Demonstration of these physiologic changes in 2 cases had led the authors to believe that biliary dyskinesia is an actual clinical entity.

They conclude that cholografin is a very important new diagnostic drug for demonstration of stones in the common duct, residual cystic duct stump, and the functional phenomenon known as biliary dyskinesia.—*Richard E. Kinzer, M.D.*

Ross, Wayne D., Finby, Nathaniel, and Evans, John A. Intramural diverticulosis of the gallbladder (Rokitansky-Aschoff sinuses). *Radiology*, March, 1955, *64*, 366–372. (Address: Dr. Ross, 525 E. 68th St., New York, N. Y.)

Protrusion of the gallbladder mucosa through the muscular layer occurs because of the lack of a muscularis mucosae and the loose arrangment of the muscular bundles. It can be graded on the basis of the depth of penetration of the gallbladder wall, and with present methods, can be demonstrated roentgenographically only after entrance into the intramuscular lacunae (grade II).

Although intramural diverticulosis is a common pathological finding, roentgenographic demonstration has been reported only 11 times previous to the 2 cases presented here (5 more have been found since this writing). The authors reviewed these 13 cases, and found that all had had histories suggestive of cholecystitis with 4 having demonstrable cholelithiasis. It is felt that visualization of intramural diverticula is an indication for cholecystectomy, since they are related to chronic inflammation and increased intraluminal pressure, and the complications of acute inflammation, cholelithiasis, and perforation may ensue.

In 7 of the 13 cases there was evidence of a construction of the gallbladder, and so their occurrence should be especially suspected when a constriction of the proximal portion of the gallbladder occurs.

Intramural diverticulosis must be differentiated from the solitary true diverticula of the gallbladder. Luschka's ducts are really hyperplastic biliary ducts and, like subperitoneal mesothelial cysts, do not communicate with the gallbladder lumen. Calculi or gas may be present in the intramural diverticula and cause diagnostic shadows outside the gallbladder lumen.—*C. L. Stevenson, M.D.*

Cancelmo, J. J. Stellate fissuring in gallstones. *Radiology*, March, 1955, *64*, 420–423. (Address: Coatesville Hospital, Coatesville, Penna.)

It has been known for years that stellate fissures occur in the centers of gallstones, and it has recently been demonstrated that these fissures may contain gas. They appear on the roentgenograms as stellate areas of radiolucency which are rather characteristic and easily recognizable.

Three cases of fissuring in gallstones are presented, in one of which the visualization of the stellate fissures on the roentgenogram was the sole basis for a diagnosis of cholelithasis.—*Harold C. Hamilton, M.D.*

Lichstein, Jacob. The differential diagnosis of benign prolapse of gastric mucosa. *Ann. Int. Med.*, Jan., 1955, *42*, 44–58. (From: University of Southern California School of Medicine, Cedars of Lebanon Hospital and Los Angeles County Hospital, Los Angeles, Calif.)

In a previous article the author correlated the clinical, roentgenologic and gastroscopic findings in a series of 52 cases of prolapse of gastric mucosa. In the present study he presents numerous case reports of other lesions of the stomach and duodenum which simulate the roentgen appearance of gastric mucosal prolapse. He lists at least a dozen conditions which might simulate benign prolapse of gastric mucosa and many of these are illustrated by case reports and reproductions of roentgenograms.

Pedunculated gastric polyp, hypertrophic gastritis, prepyloric ulcer, primary or metastatic carcinoma of the stomach, natural gastritis and diffuse gastric lesions are among the more common conditions which the author believes present difficulties in differential diagnosis. The clinical significance of gastric mucosal prolapse has indeed been much discussed during the past five years and it is certainly still a controversial subject.—*Richard E. Kinzer, M.D.*

Musgrove, J. E. Vancouver, B. C. Posterior penetrating gastric ulcer. *Canad. M. A. J.*, March 1, 1955, *72*, 342–345.

About 5–8 per cent of gastric ulcers lie in the posterior wall and tend to penetrate into the body and tail of the pancreas. The author feels that an ulcer of this type is almost invariably benign and that with careful preoperative roentgenologic study and operative palpation and inspection, the surgeon should be able to rule out malignancy in close to 100 per cent of cases.

A method of partial gastric resection which allows a Billroth I or II type of gastroduodenal anastomosis is briefly described. Four illustrative cases are presented.—*P. B. Parsons, M.D.*

Lundie, J. K., Scott, M. Gilbert, and Mackenzie, D. H. A source of error in the diagnosis of gastric malignancy. *Brit. J. Radiol.*, Feb., 1955, *28*, 95–99. (From: Westminster Hospital, London, S. W. 1.)

The authors report the case of a male, aged forty-two, in whom barium meal examination showed a persistent filling defect on the greater curvature of the stomach. Peristalsis could not be seen crossing this area and it was not altered by posture and pressure. Re-examination two hours later revealed no change. Another examination almost two months later showed that this deformity had disappeared. It was thought that the patient might have had a benign ulcer with surrounding edema which had healed in the interval, but in view of the high incidence of malignancy previously reported in greater curvature ulcers a Billroth 1 type of partial gastrectomy was performed.

The opened stomach showed a puckered scar about 2 mm. in diameter situated near the midpoint of the anterior surface. This was a healed chronic ulcer with complete fibrous replacement of muscle. There was no evidence of malignancy.

It is concluded that the irregularity seen at the first examination was produced by localized spasm of the gastric wall caused by an ulcer.—*Arthur E. Childe, M.D.*

Massik, Paul, and Wheatley, Frank E., Jr. The recognition of air in diverticula of the colon as a diagnostic aid. *Radiology*, March, 1955, *64*, 417–419. (Address: Dr. Massik, 67 Coddington St., Quincy, Mass.)

Air-filled diverticula of the colon give a characteristic image on scout films of the abdomen. They present a "bubbly" appearance—areas of slightly increased density interspersed with rounded spots of radiolucency. Their usual location is the left lower quadrant and occasionally they "string out" in a line.

Air-filled diverticula were noted on the anteroposterior scout film of the abdomen in 12 cases over a nine month period, during which time 370 barium enemas were performed. The subsequent barium enema examination failed to show diverticula at the spot suspected in only a few cases in which this sign was observed.—*Harold C. Hamilton, M.D.*

Welin, S. Zur Darstellung der Kolonpolypen mit der Doppelkontrastmethode. (The demonstration of polyps of the colon by the double contrast method.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, March, 1955, *82*, 341–344. (Address: Allmänna Sjukhus, Röntgenavdelningen, Malmö, Sweden.)

If detection of polyps in the colon is cancer prevention, the methods of finding these small tumors must be improved. The author maintains that the best possible preparation of the colon is the essential condition for the demonstration of small polyps. In his opinion castor oil and enemas are not at all efficient for that purpose. He uses a laxative, named neodrast, which belongs to the isatin preparations. This laxative acts fast and very effectively. It is given with the addition of some tannic acid in order to decrease the formation of mucus.

The author uses a somewhat thicker than usual barium mixture for the double contrast enema. The roentgenograms are taken at greater than the usual distance (120 cm.) and with a small focus tube.

Since using these modifications the results of the examination have been considerably improved. In 1,608 colon examinations polyps were found in 12 per cent; 90 per cent of these polyps were less than 10 mm. in diameter, 60 per cent less than 5 mm. This indicates the efficiency of the method. Of the 201 polyps found 65 were operated upon; 12 per cent of them were carcinomas and another 30 per cent showed precancerous changes.

The method is somewhat more troublesome and strenuous for the patients and requires more effort from the examiner, but the results are much superior to the older methods, in the opinion of the author.—*Hans W. Hefke, M.D.*

Genitourinary System

Moore, Thomas D., and Mayer, Raymond F. Hypaque: An improved medium for excretory urography. A preliminary report of 210 cases. *South M. J.*, Feb., 1955, *48*, 135–141. (Address: Dr. Moore, 899 Madison Ave., Memphis, Tenn.)

The authors present a preliminary report on the use of hypaque sodium for excretory urography in 210 cases. They feel it represents substantial progress toward the ideal medium for this purpose.

Chemically, hypaque sodium is a brand of diatriozate sodium. Studies in experimental animals reveal very low toxicity and a high degree of tolerance. It is excreted almost entirely through the kidney, most of the drug being eliminated in two hours in unchanged form.

In this series only 13.3 per cent of the patients had untoward side-effects and these were of minor character. The absence of arm pain due to vein cramps was particularly noticed. Excellent or good results from the technical standpoint were obtained in 92.9 per cent of the examinations.

The authors emphasize in their discussion that proper preparation, testing for sensitivity, slow injection and use of compression are important factors in obtaining satisfactory urograms. A laxative is given the night before the examination and fluids are withheld for twelve hours preceding the examination. Sensitivity tests consisted of injection of 1 cc. intradermally and 1 cc. intravenously. Optimum injection time for the full dose of 30 cc. was three minutes. Snug compression over the bladder applied on completion of the injection and released an instant before the first roentgenogram was obtained was used with compression re-applied for ten to fifteen minutes after each exposure was made. The authors feel that significant improvement in the pyelographic outline is obtained when compared with roentgenograms made without compression.—*Arthur B. Smith, M.D.*

Morales, Olallo, and Romanus, Ragnar. Urethrography in the male: The boundaries of the different urethral parts and detail studies of the urethral mucous membrane and its motility. *J. Urol.*, Jan., 1955, *73*, 162–171. (From: Roentgen Diagnostic Department and Surgical Department of Karolinska Sjukhuset, Stockholm, Sweden.)

A complete urethrographic study of the male urethra should include fluoroscopic and roentgenographic examinations with the lumen fully distended and micturition exposures in the anteroposterior and each oblique projection. The authors recommend the use of umbradil-viscous U (Astra). The value of such a medium is explained in detail. It is water soluble and therefore no untoward reactions occur. With such a highly viscous preparation the injection pressure is steadier and the flow more equalized. The viscosity of the preparation does not prevent it from penetrating fine ducts or capillaries. It has a low surface tension and adheres readily to the mucous membrane.

The urethra of the patient is anesthetized with a local anesthetic. Under fluoroscopic control the contrast medium is injected until the pressure overcomes the resistance of the sphincters and films are exposed in the oblique and anteroposterior projections. The patient is then instructed to contract the pelvic muscles as though he were trying to interrupt urination and films exposed in similar positions at this time. Following this, the patient is asked to strain or "bear down" and another set of films are exposed during this straining procedure. By observing the motility of the apex of the prostate during these maneuvers, one can obtain information regarding induration or fixation of the structures involved. Micturition films are exposed during the voiding process.

Twenty-three illustrations are presented showing the normal and abnormal states of the urethra in different patients.—*George W. Chamberlin, M.D.*

Comarr, A. Estin, and Bors, Ernest. Spermatocystography in patients with spinal cord injuries. *J. Urol.*, Jan., 1955, *73*, 172–178. (From: Paraplegia Service of Veterans

Administration Hospital, Long Beach, Calif., and Department of Surgery (Urology), School of Medicine, University of California, Los Angeles, Calif.)

Fifty patients who have had previous spinal cord injuries underwent spermatocystography. The objective of this investigation was to determine whether roentgenographic changes occurred in the spermatic vesicles, how much infection as manifested by white blood cells is present in the seminal washings and an analysis of the sperm. The technique is briefly outlined as follows: When necessary, local anesthesia was used for the skin incision. The vas was dissected and lifted from its bed with mild traction. The bladder was irrigated with a 5 per cent glucose saline solution. A survey roentgenogram was then taken. After this, approximately 5 cc. of glucose saline solution was injected into the vas through a No. 23 guage needle. Fifteen to 20 cc. of a 35 per cent solution of diodrast was then instilled into each vas through the needle and finally the bladder was irrigated with a 5 per cent solution of glucose and saline in order to wash out all excess opaque substance. The bladder catheter was then removed and roentgenograms were exposed. This procedure was done individually on each side and the needles were left in place in order to repeat injection when necessary. Due to pathological changes of the vas or to previous testicular operations spermatocystography was limited to a unilateral procedure in 6 patients, and on 1 patient it was impossible to make this study because the vasa were obstructed. No complications were observed following the injection of diodrast even though extravasation did occur in 1 case. In 2 patients the examination was repeated after seven months.

The interpretation of the roentgenograms was according to the classification of Pereira, and was recorded as normal, ectasia, hypoplasia or secondary atrophy. Reflux from one ejaculatory duct to the other was seen in 2 patients, filling of the prostatic cavity in 1 instance and ectasia of the ampulla of the vas was observed in 5 patients. A cyst of one spermatic vessel was encountered in 1 instance. There was no definite correlation between the spermatocystographic findings and the level of the cord injury. Hypoplasia did occur in patients with incomplete cervical and high thoracic lesions. The highest incidence of normal and atrophic findings was in the patients with complete thoracic lesions between T7 and T12. No correlation could be established between the age of the patient, the duration of the spinal cord lesion and the spermatocystographic findings. No correlation was found between the appearance of the spermatocystogram and the testicular biopsy. This latter point is of some interest because atrophy of the male adnexa might be anticipated in the absence of testicular function.

Seven roentgenograms illustrative of the normal and abnormal findings are reproduced.—*George W. Chamberlin, M.D.*

Elkin, Milton, and Mueller, H. Peter. Metastases from cancer of the prostate; autopsy and roentgenological findings. *Cancer*, Nov., 1954, *7*, 1246–1248.

The authors review 437 cases of cancer of the prostate observed from 1928 through 1948 at the Pondville Hospital, Walpole, Mass. Of these cases, 199 died and autopsies were performed on 148. Tables are included showing the frequencies as to the site of metastases, lymphatic spread, direct extension, age, and histopathological classification.

Particular reference is made to the chest roentgenogram demonstrating pulmonary metastasis and the positive autopsy finding of secondary carcinoma of the prostate in the lungs. Their findings are compared with those of other investigators and all show a very small percentage of lung metastasis demonstrated on the roentgenograms, but a rather high, 38 per cent, demonstrated at postmortem examination.

The conclusion is reached that patients dead of carcinoma of the prostate show a very high percentage of pulmonary metastases. However, only a small percentage is demonstrated roentgenographically, usually late in the course of the disease and near death.—*Thomas E. Padgett, M.D.*

Arons, Walter L., Christensen, W. R., and Sosman, M. C. Nephrocalcinosis visible by x-ray associated with chronic glomerulonephritis. *Ann. Int. Med.*, Feb., 1955, *42*, 260–282. (From: Departments of Medicine and Radiology, Peter Bent Brigham Hospital and Harvard Medical School, Boston, Mass.)

Roentgenograms of most cases of nephrosclerosis show medullary calcium deposits, irregularly rounded, of varying size, and in the regions of the medullary pyramids. Sometimes the calcification outlines the pyramid, producing a wedge-shaped shadow. This type of nephrosclerosis is found in a number of conditions.

A rarer form of nephrosclerosis is found associated with chronic glomerulonephritis only. Four cases are described in this report. The calcification is fine, diffuse and strikingly predominant in the renal cortex. Only 2 other similar cases were found in a review of the literature. Histologically, the calcification was found mostly in the tubular lumina and to a lesser degree in the lining tubular epithelium. A history of excessive calcium ingestion was found in 5 of the 6 cases. Though not frequently encountered, nephrosclerosis predominant in the renal cortex appears to represent weighty evidence in favor of chronic glomerulonephritis.—*George Cooper, Jr., M.D.*

Engel, William J. Symposium on retroperitoneal tumors. Classification of retroperitoneal tumors as a guide in clinical diagnosis. *A.M.A. Arch. Surg.*, Feb., 1955, *70*, 156–160. (From: Department of Urology, Cleveland Clinic Foundation, and Frank E. Bunts Educational Institute, Cleveland, Ohio.)

The author presents a classification of retroperitoneal tumors, designed primarily as an aid to clinical diagnosis, as the first paper in a symposium devoted to discussion of such tumors. He places all retroperitoneal tumors in three broad categories: (1) primary unattached tumors, (2) tumors arising in organs normally present in the retroperitoneal space, and (3) primary or metastatic tumors involving the retroperitoneal lymph nodes.

The primary unattached tumors, he states, are no longer considered rare. They may be benign or malignant; solid, cystic, or both; single or multiple; and of varied histologic type. Recurrence following surgical removal is common, and a tumor originally regarded as benign may recur as a malignant tumor. The tumors are considered to arise chiefly from embryological remnants of the urogenital tract.

Renal tumors of various types constitute the largest group of retroperitoneal tumors. Benign tumors include adenomas, serous cysts, polycystic disease, congential hydronephrosis, pyonephrosis, cortical abscesses, and hematomas. Malignant tumors embrace hypernephromas or clear cell carcinomas, sarcomas, Wilms's tumors, and tumors of the renal pelvis.

Adrenal tumors may be either medullary or cortical in origin. The medullary tumors include neuroblastomas and pheochromocytomas. Cortical tumors may be adenomas or carcinomas. Pancreatic tumors include cysts and carcinomas.

Primary retroperitoneal tumors of lymph nodes are uncommon, and are usually classified as "lymphomas." Metastatic tumors may involve the paraaortic lymph nodes from the testes, ovaries, or intraperitoneal organs. —*Edgar C. Davis, M.D.*

Steinbach, Howard L., and Smith, Donald R. Extraperitoneal pneumography in diagnosis of retroperitoneal tumors. *A.M.A. Arch. Surg.*, Feb., 1955, *70*, 161–172. (From: Departments of Radiology and Urology, University of California School of Medicine, San Francisco, Calif.)

The authors have used extraperitoneal pneumography to demonstrate tumors of the adrenal glands and of the kidneys. They believe that its greatest usefulness is in examination of the adrenal glands. They agree with other investigators that the procedure is relatively harmless. Gas, preferably oxygen, is injected into the areolar tissue between the rectum and the sacrum and is allowed to spread throughout the extraperitoneal tissue.

The kidneys and adrenals are encased in a loose fascial sheath known as "Gerota's capsule," which is fused superiorly and laterally but is open medially and inferiorly. Injected gas ordinarily will fill the sheath as well as pass around it, thus visualizing the encased kidneys and adrenals. The kidneys lie loosely in the sheath, but the adrenal glands are more firmly attached in its apex. From molding of adjacent structures the right adrenal gland is triangular and the left semilunar in shape.

The edge of Gerota's capsule is well seen on laminagraphy as a thin membrane, and is helpful in differentiating masses of adrenal and renal origin, from tumors and cysts of adjacent organs.

The authors have devised a method of measuring the size of the adrenal gland in an effort to establish a normal. A compensating polarimeter was employed. The average cross-sectional area was found to be 4.2 sq. cm. on the right side and 4.3 sq. cm. on the left. No significant difference was found in sizes of adrenals in males and in females.

In cortical hyperplasia the adrenal glands are enlarged bilaterally without change in shape, the right adrenal having an average area of 12 sq. cm., and the left 12.3 sq. cm. The diagnosis of cortical hyperplasia by pneumography proved extremely difficult in some cases.

Four cases of adenoma of the adrenal gland are described. The involved gland showed spherical enlargement and the opposite uninvolved gland always was small.

In the one case of malignant neoplasm presented, pneumography failed to outline the adrenal. Pheochromocytomas could not be differentiated from adenomas or encapsulated carcinomas by pneumography. These tumors all appeared as spherical enlargements of the adrenal glands on the pneumogram. The authors feel that under certain circumstances, and with proper clinical and laboratory correlation, bilateral small adrenals can indicate a secretory tumor in the gonads.

Pneumography proved useful in demonstrating kidney tumors in which a complete ureteral block prevented the use of pyelography. Noninvasive malignant renal tumors could not be differentiated from renal cysts. Invasive malignant tumors, inflammations and scarring tended to prevent the gas from ascending into the region of the kidney.

Pneumography was used to some advantage in localizing and diagnosing a reticuloendothelial hyperplastic mass, Hodgkin's disease involving the retroperitoneal space, metastases to aortic and celiac lymph nodes, large cysts of the head of the pancreas, and cysts of any size in the tail of the pancreas.

Seventeen institutions using extraperitoneal pneumography were canvassed by questionnaire. Reports thus obtained on a total of 1,995 pneumo-

grams, including 350 of the authors' series, showed no deaths and no serious complications from this procedure. Information from other sources revealed two instances of death, one of hemiplegia, and one of severe shock following presacral gas injection. Brief histories of these 4 cases are presented. It is pointed out that in the cases of both fatalities, room air instead of oxygen had been used. The authors advise against the use of the knee-chest position for introducing the gas, and favor injection with the patient in the lateral recumbent position.—*L. E. Sargent, M.D.*

Berry, John F., Robbins, John J., and Pirkey, Everett L. Abdominal aortography. *A.M.A. Arch. Surg.*, Feb., 1955, *70*, 173–177. (From: Department of Radiology and Section on Urology, University of Louisville School of Medicine, Louisville, Ky.)

Abdominal aortography is presented as a useful method of differentiating intrarenal and extrarenal retroperitoneal masses, and as a helpful aid in differentiating benign and malignant tumors of the kidney.

The authors' technique is described.

Cases of aortic aneurysm, pheochromocytoma, hepatoma, renal cyst, and malignant tumors of the kidney are reported and illustrated.

The authors believe that renal-cell carcinoma of the kidney gives a diagnostic roentgenographic appearance of pooling and "laking" during aortography which is not found in papillary carcinomas of the kidney and pelvis.—*L. E Sargent, M.D.*

Fulton, Harold, and Evans, William A., Jr. Roentgen examination in retroperitoneal tumors of children. *A.M.A. Arch. Surg.*, Feb., 1955, *70*, 178–190. (From: Department of Radiology, Childrens Hospital of Michigan, Detroit, Mich.)

Among 74 cases of retroperitoneal tumor encountered at the Childrens Hospital of Michigan in the period 1940 to 1953, adequate pathologic and roentgenologic studies were available in 53. These included 25 renal embryomas (Wilms's tumors), 23 abdominal neuroblastomas, and 5 retroperitoneal teratomas.

The average age at admission for Wilms's tumor and neuroblastoma patients was about the same. The peak incidence for the former, however, was at about three years; that for the latter between one and two years. Wilms's tumors rarely occur after the age of six years, whereas neuroblastomas may be found throughout childhood and adult life. The teratomas were all found before the age of one year. There was no significant sex or race preponderance.

An abdominal mass was a prominent sign in all patients having any of the 3 tumors. Hematuria was a symptom in 3 patients with Wilms's tumor, but in none of the patients having neuroblastoma. In neuroblastoma patients, systemic symptoms frequently were due to metastases. An elevation of temperature above 100°F. was frequent in patients with Wilms's tumors, not with the other conditions.

It is urged that roentgenographic studies be made in every case, not only of the kidneys but also of the chest, long bones, and skull. Excretory urography is proposed in preference to cystoscopy and retrograde urography. Perirenal air injection, retroperitoneal emphysema, pneumoperitoneum, and aortography were not utilized in any of the 53 cases. Calcification was visible in 2 of the Wilms's tumors (8 percent) in the form of linear plaque-like calcifications at the peripheries; in 11 of the neuroblastomas (47 per cent) as either flocculent punctate areas throughout the mass or linear deposition at the circumference. Calcified cartilage and bone were demonstrated in 3 of the 5 patients having retroperitoneal teratomas.

Maintenance of the outline of the kidney, in the presence of a retroperitoneal mass demonstrable clinically or roentgenologically, was rare in the cases of Wilms's tumors, was common with the neuroblastomas, and was invariable with the teratomas. Displacement of the kidney or kidneys occurred with all 3 tumors. Medial and upward kidney displacements were not seen in the neuroblastoma patients, but were fairly common in the renal neoplasm patients. An intrarenal mass was encountered at urography in 88 per cent of Wilms's tumor patients, in only 33 per cent of neuroblastoma patients, and in none of the teratoma patients.

Metastases were not found in the teratoma patients. In the others they were common, but their distribution differed significantly. In at least one-half of the 25 Wilms's tumor patients there was intra-abdominal extension of the tumor outside the bounds of the kidney or metastatic spread to other abdominal organs, but these metastatic components could not be documented roentgenologically. Only 2 of the 25 showed metastases by roentgenographic study, in the lung parenchyma. No case of osseous spread of Wilms's tumor was present.

The neuroblastomas showed metastatic involvement of liver, kidney, mediastinum, and skeleton. No lung metastases were disclosed roentgenologically although autopsy of one patient revealed lung involvement by tumor which was considered to be a terminal event. Among 19 patients in whom the skeleton was surveyed, bone metastases were found in 9—7 generalized and 2 focal. The bone lesions most typically were found in the submetaphysial regions of the long bones, and, in contrast to the situation in leukemia, rarely involved the metacarpal and metatarsal bones.—*Edgar C. Davis, M.D.*

Evans, Arthur T. Combined use of contrast media in retroperitoneal tumors; critical evaluation. *A.M.A. Arch. Surg.*, Feb., 1955, *70*, 191–198. (Address: 1908 Union Central Building, Cincinnati, Ohio.)

A critical evaluation is presented with the author expressing the opinion that the combined use of contrast media in retroperitoneal tumors is not warranted, sometimes is confusing, technically more difficult, increases the risk to the patient, and frequently results in loss of time, material and money. The combination of pyelography and perirenal gas, although producing an appealing roentgen visualization, is frequently not diagnostic. He has not found it necessary to combine pyelography and periadrenal gas to demonstrate adrenal enlargement, feeling it unnecessary to repeat the pyelogram at the time of gas introduction. Since arteriography is of no value in the diagnosis of adrenal tumors, its combination with retroperitoneal gas for the study of adrenal masses is worthless. In the case of extravisceral retroperitoneal tumors, the lesions may be delineated by retroperitoneal gas, which, however, is useless in differentiating primary tumors of the kidney from extrarenal masses attached to its surface. The addition of pyelography, will show only displacement or juxtaposition and the two procedures do not show whether the mass is renal or extrarenal in origin.

Although arteriography is of proved value in the diagnosis of renal parenchymal tumors and cysts, it produces no diagnostic pattern in the extrarenal tumors unless they have extensively invaded the renal parenchyma, and has not proved useful in the diagnosis of adrenal tumors. Combining the arteriogram with any other procedure would be of no value if the arteriogram alone does not possess diagnostic accuracy for the lesion in question. The addition of retroperitoneal air to the arteriogram in the case of renal tumor or cyst, may produce confusing roentgen images, difficult to interpret. Retrograde pyelography in combination with arteriography may produce gratifying results in the diagnosis of renal tumors but too infrequently the pyelographic medium obscures the arterial pattern. The study of adrenal tumors by arteriography and pyelography is valueless since neither produce's characteristic changes.—*Thomas F. Meaney, M.D.*

Costolow, William E., and Wisdom, William R. Radiation therapy in retroperitoneal tumors. *A.M.A. Arch. Surg.*, Feb., 1955, *70*, 199–202. (From: Los Angeles Tumor Institute, Los Angeles, Calif.)

The authors present results of radiation therapy in 73 patients with retroperitoneal tumors treated at the Los Angeles Tumor Institute from 1930 to 1953. Some of the patients were treated in the immediate postoperative period, whereas others were treated much later either for local recurrences or metastases.

Fifty-two of the tumors were of renal origin, ten were primary retroperitoneal tumors and eleven were lymphosarcomas.

The authors attempted to deliver 2,200 r in thirty-two days to the adenocarcinomas of the kidney, and the same dosage in twenty-six days to pulmonary metastases. They believed that approximately 3,000 r in thirty to forty days was adequate treatment for Wilms's tumors in children, and 5,000 to 6,000 r in thirty-five to forty days for adults. In each case that treatment field covered the entire abdomen.

For primary retroperitoneal tumors the doses varied from 2,500 to 5,200 r, depending on the patient's tolerance.

The lymphosarcomas showed the most favorable results and were treated with small initial doses from 75 to 100 r per day, then increased to about 170 r per day to a total of 3,500 to 4,000 r.

The authors state that a significant increase in survival time can be obtained by adequate irradiation. They encountered difficulty in estimating the prognosis because of the varied origin of the tumors and their unpredictable response to irradiation. They believe that the majority of retroperitoneal tumors are radiosensitive and will show some degree of response to radiation therapy.—*D. V. Campbell, M.D.*

Tidrick, R. T., and Goldstein, M. S. Surgical treatment of retroperitoneal tumors. *A.M.A. Arch. Surg.*, Feb., 1955, *70*, 203–206. (From: Department of Surgery, State University of Iowa, College of Medicine, Iowa City, Iowa.)

The authors report on 32 cases of surgically removed primary retroperitoneal tumors encountered between 1946–1954. This series excluded sacrococcygeal teratomas and tumors of renal, pancreatic, or adrenal origin.

Preoperative preparation of the patient is discussed as well as the value of roentgenographic studies for determining the location and extent of the neoplasm. The studies included plain films of the abdomen, urographic and gastrointestinal examinations, and in many instances angiography. Pneumography was utilized principally in connection with adrenal tumors.

At operation the authors used neurosurgical clips to delineate the boundaries of the neoplasm in the event that subsequent roentgen therapy was undertaken. They preferred to have the radiotherapist witness the gross findings at surgery whenever possible. They believe that postoperative irradiation should not be started until gastrointestinal function has returned to normal.

Of the 32 cases reported, only 10 were resectable, and of these only 3 were treated with postoperative irradiation.—*D. V. Campbell, M.D.*

Baronchelli, A., and Rossi, L. Retropneumoperitoneo e stratigrafia nella semeiologia delle ghiandole surrenali. (Retropneumoperitoneum and stratigraphy in the symptomatology of the suprarenal glands.) *Ann. radiol. diag.*, 1954, *27*, 261–297. (From: Istituto di Patologia Speciale Medica dell' Università, Bologna and Istituto di Radiologica dell'Università, Firenze, Italy.)

Because of their small size, their position just above the upper poles of the kidneys, and the nature of the surrounding and overlying structures, suprarenal glands are difficult to demonstrate on conventional roentgenograms. Retropneumoperitoneum as advised by Ruiz-Rivas in 1947 has permitted study of the size and shape of the suprarenal glands in more detail. The addition of laminagraphy does away with disturbing superimposed shadows.

The authors give considerable attention to the preliminary preparation. The patient is placed on a low residue diet, with fasting for twelve hours before the examination. A glycerin and water enema is given the day before. The procedure is done under local anesthesia and mild sedation. Oxygen is injected with the patient in a prone position with elevation of the hips above the head. In children 300–500 cc. of O_2 are used, in adults larger amounts, 1,000–1,600 cc. Within the first or second hour after the oxygen injection, the gas has permeated the structures about the renal and suprarenal area. Laminagraphic examinations are made at 1 cm. layers between the 4–10 cm. level measured from the back. These latter films are exposed with the patient either in a supine or erect position.

The adrenal glands vary in size and shape in normal individuals making it difficult to distinguish minor changes. They are especially difficult to identify in children.

The following are the indications for the use of this combined type of examination: (1) adreno-genital syndrome—with hyperfunction of the adrenal cortex due to either hyperplasia, adenoma or carcinoma of the gland; (2) Cushing syndrome; (3) obscure syndromes (adrenogenital and Cushing syndrome); (4) paroxysmal hypertension pheochromocytoma, and (5) Addison's disease and cases of adrenal insufficiency showing either reduction in size of the adrenal gland or calcium deposits about the gland.

The authors report 10 cases in detail with history, physical and laboratory findings. Correlation of all data is most important for proper evaluation of the case under consideration.

The following conclusions are reached: The normal adrenal glands have a low degree of opacity as shown by this special technique. Their outline is more or less irregular and somewhat triangular. They are usually detached from the upper pole of the kidney. The right adrenal is located at a lower level than the left adrenal and is in a medial position and looks somewhat larger. Prolongations of the gland extending upward along the adrenodiaphragmatic ligament are not unusual.

The shadows observed on the film are due to the substance of the gland itself, the surrounding fatty tissue and the fascial ligaments. An increase in opacity of the gland has a certain significance, permitting better visualization. The authors believe this to be an important finding in pathological cases. Increase in the size of the gland is likewise of diagnostic value especially if the opposite gland remains normal. If the gland increases in size only and retains its shape a hyperfunction may be suspected. An increase in size associated with change in shape is more indicative of an adenoma or neoplasm. In case of Addison's disease both adrenal glands may be reduced in size and minute calcium deposits may be present within the gland substance.—*Peter E. Russo, M.D.*

Lurà, A., Forni, G., and Biavati, C. Le immagini dei surreni ottenute con insufflazione retroperitoneale al controllo operatorio. (Images of the suprarenals obtained with retroperitoneal insufflation and controlled by surgery.) *Ann. radiol. diag.*, 1954, *27*, 298–351. (From: Istituto di Radiologia e di Patologia Chirurgica dell'Università, Bologna, Italy.)

The authors describe the roentgen findings in 300 cases of normal and pathological adrenal glands, examined by retropneumoperitoneum associated with laminagraphy and in a few instances with excretory urography. In 40 of these cases, which came to surgery, correlation between the roentgenological and surgical findings was possible.

It was found that after retropneumoperitoneal insufflation the adrenal gland is displaced upward and away from the upper pole of the kidney. A wide variation in size and shape of the gland was noted even in normal individuals. When disturbing shadows were present in the suprarenal area, laminagraphy with the patient in the upright position gave the best results.

In pathological cases, when the adrenal gland is increased in size or density and shows changes in shape or when there are calcifications present, laminagraphic study alone without the aid of air insufflation is sufficient to obtain good visualization.

An increase in size accompanied by an increase in density of the adrenal gland must be considered as being pathological regardless of whether the changes occur on one side or both sides. Enlargement and deformity of the adrenal gland on one side points to the presence of a tumor, especially if the gland appears spherical in shape.

The tail of the pancreas may be superimposed on the left adrenal gland and may be mistaken for a tumor of the gland.

The authors observed a case of Buerger's disease with an adenoma of the adrenal gland which was removed surgically but no follow-up was made of the result obtained.—*Peter E. Russo, M.D.*

Skeletal System

Chambers, William R. Headache as the first and only sign of basilar impression. *J. Bone & Joint Surg.*, Jan., 1955, *37-A*, 189–192.

During the course of study concerning the cause and treatment of severe intractable headache in the occipital area, the author found that an unusual number of the cases severe enough to warrant operation showed pathological lesions in and about the atlanto-occipital area. Five of these patients had platybasia or basilar impression without neurological symptoms other than headache. In these 5 cases operated upon, basilar impression was proved by roentgenograms and operation. In 3 of the cases, there was almost total relief of pain, and in 2 cases, in which the suboccipital decompression was not done in spite of the basilar impression, little relief was obtained.

The author suggests that in cases of severe occipital headache, roentgenographic search for the possibility of basilar impression is advisable.—*Ralph S. Bromer, M.D.*

Meiss, W. C. Spinal osteotomy following fusion for paralytic scoliosis. *J. Bone & Joint Surg.*, Jan., 1955, *37-A*, 73–77.

In some cases, surgery of the vertebral column constitutes the last possibility of correcting deformities. The author's experience with vertebral osteotomy in the treatment of ankylosing spondylarthritis, as first reported by Smith-Petersen and later by la Chapelle, induced him to resort to lateral wedge osteotomy on the convex side in a female patient who had been almost completely disabled by severe lumbar scoliosis.

The result of the operation is shown in roentgenograms. Although the author does not consider the end result to be entirely satisfactory—the patient's back is not completely straight—he feels that this operation is indicated in the rare case in which the patient is severely disabled by scoliosis. Some of the dangers which must be avoided are: (1) injury to the posterior nerve roots; (2) injury to the cord; (3) artificial spondylolisthesis during or after the operation which may result in the two injuries mentioned. Obviously, because of the great hazards involved, the operator should have a detailed knowledge of the regional anatomy, as well as extensive experience in operations on the vertebral column—*Ralph S. Bromer, M.D.*

Schlesinger, Philip T. Incarceration of the first sacral nerve in a lateral bony recess of the spinal canal as a cause of sciatica. *J. Bone & Joint Surg.*, Jan., 1955, *37-A*, 115–124.

The purpose of this article is to describe a bony recess in the spinal canal at the level of the fifth lumbar and the first sacral vertebrae to discuss its possible clinical significance in the causation of sciatic pain, and to relate this to the general problem of root compression in the lower lumbar region. Normally a bony recess exists at the level of the fifth lumbar and the first sacral vertebrae medial to the intervertebral foramen, the posterior wall of which is formed by the superior articular process of the sacrum and the anterior wall by the fifth lumbar vertebral body and disk. In certain subjects this recess is considerably deeper, the posterior wall extending toward the midline. When the first sacral nerve becomes incarcerated in this recess, compression results, with consequent production of sciatic pain. So far as the author is aware, the presence of a deep recess in this area and its role in the compression of the first sacral nerve have not been previously described.

The lateral recess may be narrowed from before backward by degeneration and thinnning of the fifth lumbar disk, especially if there is backward displacement of the body of the fifth lumbar vertebra or if there is a hypertrophic rim on its inferior border. The first sacral nerve can be caught in this recess and sciatica may result. Compression of the first sacral nerve in the lateral recess or of the fifth lumbar nerve in the intervertebral foramen should be considered as possibilities in patients of about fifty or over suffering from sciatica, especially if roentgenograms show thinning of the fifth lumbar disk.

When compression of a nerve has taken place lateral to the dura in the lateral recess or intervertebral foramen, whether by disk protrusion or by impingement of bone or other structures, myelography will probably not be useful and a negative myelogram cannot rule out such possibilities.

The author suggests that it is advisable to conceive of disk surgery at the age of fifty or more years in terms of root exploration rather than simple removal of a herniated disk.—*Ralph S. Bromer, M.D.*

Adkins, E. W. O. Spondylolisthesis. *J. Bone & Joint Surg.*, Feb., 1955, *37-B*, 49–62.

This article is based on a review of 46 cases operated upon by the author during the past five years. With this information he has attempted to correlate the symptoms with the anatomical findings, and hence to provide a logical approach to the treatment of the conditions.

The symptoms of spondylolisthesis fall broadly into two groups, backache and pain referred to the lower limbs. The backache has usually and probably correctly been attributed to the instability of the affected segment which increases the strains on the

intervertebral ligaments and joints and ultimately causes severe localized osteoarthritis. The cause of the radiating pain to the lower legs is a much more controversial subject, and in recent years many suggestions have been put forward to explain its occurrence. One theory is that pain from a local lesion in muscle, ligament or joint will be referred to area of skin supplied by the same segmental nerve. No one has, however, succeeded in showing what this elusive local lesion may be. In favor of the theory that radiating pain is caused by direct interference with the nerve root, there is the indisputable fact that sciatica can be produced by compression of the root by a prolapsed intervertebral disk, or by rare or anatomically similar lesions such as a nerve root tumor, and that it can be relieved immediately and absolutely by removal of the lesion causing compression. However, it must now be accepted that many cases of sciatica are not due to prolapsed disks and other causes of a mechanical nature of root compression must be searched for which might produce similar pain.

The morbid anatomy of the condition is discussed in the article under the heading spondylolisthesis with laminal defects, which includes the lamina, the pseudarthrosis, the disk and the intervertebral foramen. Changes the author has found at operation are described. He believes the most important possible causes of root irritation are the laminal pseudarthrosis, the narrowing of the neural groove found in cases with scarring of the disk, and the forwardly displaced facets found in cases with laminal defects. Factors which might irritate the root rather than compress it must be searched for. During movements of the spine the nerve root glides within its bed and constriction or irregularities of this bed are likely sources of such irritation. The effect of such factors would be greatly increased by adhesions which fix the root at one point, so that it is undergoing constant traction.

In association with spondylolisthesis, 2 cases of tuberculosis occurred in the author's series. In 1 of these cases the deformed segment was only involved. One case had bladder dysfunction and saddle anesthesia. This was an atypical case of spondylolisthesis with intact lamina in which slipping had occurred as a result of congenital deficiencies in the inferior facets. Previous authors have reported cauda equina lesions resulting from spondylolisthesis.

In regard to etiology, the theory of developmental defects as a cause, is supported by the occurrence of double lesions in 2 of the author's cases and by its association with spina bifida in 3 cases.

Adequate decompression of the affected nerve root is esssential in all cases with sciatic pain and the operative procedure is described in the article. The problem of arthrodesis is to be discussed in a separate article.—*Ralph S. Bromer, M.D.*

Pimm, Lionel H. Tuberculosis of the subdeltoid bursa; a review, with a report of two cases. *J. Bone & Joint Surg.*, Feb., 1955, *37-B*, 102–106.

Tuberculosis of the shoulder joint represents less than 1 per cent of all bone and joint tuberculosis and affection of the subdeltoid bursa is still less common. It receives scant if, indeed, any mention in current British and American orthopedic textbooks. Two cases are reported in this article. In earlier reported cases "cysts" containing rice bodies were found when the bursae were excised. The fibrinous nature of the rice bodies was first demonstrated by Virchow in 1856 who began the controversy on the mode of their formation. It is now generally accepted that rice-body formation is not peculiar to tuberculous bursitis.

Tuberculosis of the subdeltoid bursa, although rare, is a distinct entity according to the author, and if the diagnosis is borne in mind it should be possible to differentiate it from nonspecific bursitis on the basis of the symptoms, clinical examination and roentgenographic findings. The condition is of insidious onset and a year or more may pass before advice is sought. Pain does not appear to be a prominent feature in the early stages and is often more in the nature of a feeling of stiffness. Constitutional signs are absent unless there is an active tuberculous focus elsewhere in the body. There is local swelling of the shoulder, associated in some instances with crepitation, tenderness and increased warmth. Limitation of movement, although reported in the literature was not pronounced in the author's 2 cases reported here, and it seemed mechanical in origin. Diagnostic aspiration is useful because isolation of the tubercle bacillus allows chemotherapy to be begun before operation.

In the cases reported, roentgenographic examination showed changes in both the acromion and the greater tuberosity of the humerus. At operation the bone appeared healthy, and, as pointed out by previous authors, such changes probably represent rarefaction from local hyperemia rather than tuberculous involvement of the bone.

The treatment of choice is radical exision of the bursa if the patient's general condition allows. Ideally, streptomycin combined with one or more or the other available antituberculous drugs should be begun before exploration—*Ralph S. Bromer, M.D.*

Ingram, Alvin J., and Turner, Thomas C. Bilateral traumatic posterior dislocation of the hip complicated by bilateral fracture of the femoral shaft; report of a case. *J. Bone & Joint Surg.*, Dec., 1954, *36-A*, 1249–1255.

The combination of bilateral traumatic dislocation of the hip and bilateral fracture of the femoral shaft has not been reported previously in the literature so far as could be ascertained by the authors.

They present the case reported in this article for this reason and also because of the excellence of the result obtained by treatment.

The patient, a seventeen year old white male, was injured in an automobile accident. He was riding in the right front seat at the time of the accident, and the car was hit head on by another automobile. The patient was driven forward by the impact so that his knees struck the dashboard and then his body was thrown through the right front windshield. In addition to the mild cerebral concussion, multiple contusions and abrasions, he was found to have sustained bilateral posterior dislocation of the hip and bilateral fracture of the femoral shaft. The closed fracture of the left femoral shaft was in the proximal portion of the middle third, while on the right side, the fracture was open, penetrating the skin through a pin-point opening at the junction of the middle and distal thirds of the femoral shaft.

An excellent result was obtained following closed reduction of the dislocated hips and secondary open reduction and medullary nailing of the femoral fractures. Photographs taken twenty-one months after the injury demonstrated complete range of motion in both hips and equal lengths of the lower extremities. The only residual disability was incomplete paralysis of the left sciatic nerve with mild footdrop which did not require the use of a brace.

Dislocation of the hip complicated by fracture of the neck of the femur and dislocation complicated by intertrochanteric fracture and also by fracture of the shaft have been reported but no case could be found of bilateral dislocation with bilateral fracture of the shaft.—*Ralph S. Bromer, M.D.*

Abbott, LeRoy C., and Lucas, Donald B. Arthrodesis of the hip in wide abduction. *J. Bone & Joint Surg.*, Dec., 1954, *36-A*, 1129–1140.

Arthrodesis of the hip is often difficult to obtain, even under the most favorable conditions. The frequent failure to obtain bony fusion in cases where joint destruction was severe led the authors to the development of the treatment which they called "arthrodesis of the hip in wide abduction." The method as they originally described it was done in three stages: (1) correction of the deformity, (2) arthrodesis of the hip in wide abduction, and (3) reduction of the widely abducted position by subtrochanteric osteotomy. The usual deformities of flexion, adduction and shortening were corrected by appropriate traction as the extremity was gradually brought to a position of wide abduction. In the article the operation is described in detail, other methods which have been reported are discussed, 2 cases are reported and illustrative roentgenograms are reproduced, showing end results.

In their summary, the authors state that their method provides the following conditions favorable to union: a large area of contact between cancellous bone surfaces with excellent circulation, firm apposition, and good immobilization. Important to the maintenance of contact at the site of fusion is the axial impaction provided by the tightness of the abductor muscles.—*Ralph S. Bromer, M.D.*

Lloyd-Roberts, G. C. Osteoarthritis of the hip; a study of the clinical pathology. *J. Bone & Joint Surg.*, Feb., 1955, *37-B*, 8–47.

In this study of osteoarthritis of the hip two aspects of the condition are discussed, namely, the attempt to relate the symptoms with the morbid anatomy of the disease and secondly, consideration of the factors that predispose to its development. The four possible structures from which pain may arise in diseased joints are the articular cartilage and underlying bone, capsule and synovial membrane, the surrounding muscles, and (in the hip joint) the periosteum investing the intracapsular bone. The clinical, operative and histological study of the synovial membrane and capsule of 25 patients suffering from osteoarthritis of the hip of sufficient severity to require operation led to the following conclusions: (1) The synovial membrane is abnormally congested and villous, and the capsule and subsynovial connective tissue are fibrotic. (2) The subsynovial and capsular fibrosis is a response to sustained synovial hyperplasia and congestion. (3) In osteoarthritis both the synovial hyperplasia and capsular fibrosis are due very largely to the presence of articular debris which can be seen lying beneath the surface layer of the synovial membrane. The debris arise from the degenerate joint surfaces and are removed by the synovial membrane. (4) Gravity appears to direct most of these fragments to the synovial pocket below the neck of the femur so that it is usual to see the greatest amount of synovial congestion in that area. It is probable that capsular fibrosis and shortening begin there, though they later spread to involve the entire capsule of the joint. (5) Many of the symptoms and signs of osteoarthritis of the hip are due to this fibrosis which interferes with the normal function of the joint capsule. It has been shown by Walmsley that the whole capsule is tight in the position of extension with some abduction and medial rotation. This is the position of greatest stability on weight bearing. Shortening of any part of the capsule will suppress this position and at the same time expose the capsule to stretching produced by the force of body weight. If this shortening occurs inferiorly not only will extension be inhibited but (for anatomical reasons) also medial rotation and abduction. Further shortening will cause deformity toward the position of flexion, adduction and lateral rotation. (6) This deforming property of the capsule is reinforced by reflex guarding in the muscles supplied by the motor branches of sensory nerves to the lower part of the joint cavity, such as the pectineus, quadratus femoris and the

adductor group. This dynamic deformity is later followed by a structural deformity from fibrosis at the musculotendinous junction. (7) Capsular fibrosis by preventing the hip joint from extending (in which position there is the largest area of femoral articular cartilage in contact with the acetabulum) may tend to speed deterioration in a degenerate joint.

The second section of the article deals with the morbid anatomy and clinical significance of some of the skeletal changes in osteoarthritis. Observations were based on a clinical study of arthritic hip joints subjected to operation, 131 in number. Most authorities agree that the articular cartilage shows earliest evidence of joint degeneration and that, by the time this has progressed sufficiently to cause symptoms, the greatest loss is found to have occurred in that area of the femoral head on the upper quadrant which is in contact with the acetabulum when the joint is bearing weight or moving within a moderate range. While these changes are taking place on the surface of the articular cartilage the deeper layers are undergoing modification: cracks extend from the surface as far as the subchondral plate, the cells enlarge and there is widening of the normal basal layer of calcified cartilage. Of clinical significance are the facts that (1) the fragments of cartilage become detached and are subsequently absorbed within the synovial membrane which causes synovial hyperplasia and later capsular fibrosis, and (2) the widening of the calcified zone of the cartilage and the formation of new bone superficial to the subchondral plate account for the "subchondral sclerosis" seen in the clinical roentgenograms in early stages of osteoarthritis.

Initially the subchondral bone becomes more vascular and granulation tissue fills the spaces between the bone trabeculae in the area below the greatest cartilage damage. Some of this granulation tissue passes through the subchondral plate, but for the most part it seems to be concerned with bone remodelling through the activity of the osteoblasts and osteoclasts which it contains or by metaplasia. The cause of these striking changes is obscure but it seems probable that they represent the reaction of bone, deprived of the protection of articular cartilage, to the stress of weight bearing and activity.

Cysts were found in every one of the femoral heads examined in the area where the cartilage has suffered most. In consequence they lie within that part of the subchondral zone which is eburnated or in which new bone is being laid down. They frequently communicate with the surface through narrow channels which are visible as pits on the surface of eburnated bone. The author's observation favors the view that the cysts arise as a result of a failure in the remodelling process, so that osteoclasis outstrips osteoblastic activity in certain areas. Cysts visible in the roentgenogram usually indicate painful arthritis. They, like eburnation, only occur when degeneration is advanced which accounts to some extent for their association with painful arthritis. They may also contribute to the amount of joint debris through their surface communications. Their most significant effect, however, is to weaken the articular surfaces so that the hip can subluxate more readily, particularly if the collapse is associated with a previous loss of bone so that the weight-bearing areas of the femoral head and acetabulum are no longer opposing segments of a circle.

Many cases of advanced osteoarthritis show roentgenographic evidence of new bone formation on the under surface of the femoral neck. The author suggests that this ridge is due to the deposition of new bone within a subperiosteal space produced by traction transmitted through the fibrotic capsule to the periosteum invading the neck.

Osteophytes are a conspicuous feature of osteoarthritis. They are found either upon that part of the femoral head or acetabulum which is neither concerned with weight bearing nor movement within the habitual range, or as a ring around the junction of the articular cartilage of the head with the neck of the femur. The clinical significance of osteophytes is far less than their conspicuous nature would suggest.

Four aspects of the etiology and pathogenesis of the disease are discussed in the article. Incongruity between the articular surfaces of the femoral head and the acetabulum is a recognized cause of osteoarthritis. In this series there were 15 (12.1 per cent) osteoarthritic hips attributable to this, 8 of adolescent coxa vara with uncorrected deformity, 3 of Perthes' disease with imperfect reconstruction of the femoral head, 2 of protrusio acetabuli, and 1 each of coxa vara complicating Paget's disease and intertrochanteric fracture. The mechanism of this is discussed in detail in the article.

Congenital dysplasia is important not only as a cause of osteoarthritis of the hip joint but also because its early recognition presents an opportunity to prevent the disease from developing. A shallow acetabulum can be corrected or improved in youth by treatment in abduction. As judged by a small series of cases, the earlier the treatment is begun, the better is the outlook for the acetabulum.

The supposition that osteoarthritis is commonly due to progressive ischemia in the femoral head was investigated and was rejected as a cause by the author.

The cause of idiopathic osteoarthritis remains obscure but the evidence suggests that constitutional rather than local conditions in the joint account for many cases of this type.—*Ralph S. Bromer, M.D.*

Harrison, R. G., and Gossman, H. H. The fate of radiopaque media injected into the cancellous bone of the extremities. *J. Bone & Joint Surg.*, Feb., 1955, *37-B*, 150–156.

It has been known since 1943 that solutions injected into cancellous bone are rapidly removed into the venous system. Observations were made by the authors on the cadavers of 3 men and 3 women, aged forty-six, fifty-three, sixty-one, sixty-three, sixty-eight and seventy-six years, death being due to coronary thrombosis in 3 cases, bronchopneumonia in 2 cases and carcinoma of the bronchus in 1 case. The experiments were performed forty-eight to seventy-two hours after death. The method of injection was the employment of a sternal or lumbar puncture needle ground so as to produce a symmetrical sharp point which was pushed through the skin and tapped into the underlying bone with a hammer. The trocar was withdrawn quite easily once it has perforated the compact bone and was imbedded within the cancellous bone. Until then the trocar could not be withdrawn except with force. A syringe was attached to the needle and radiopaque medium was injected.

In several instances dissections were performed immediately after injection and roentgenograms were made to determine exactly the route of drainage. Sites of injection were the acromion process of the scapula, the head of the humerous, the olecranon process of the ulna, the ilium and greater trochanter of the femur, the proximal end of the tibia and the medial malleolus.

The authors were able to confirm the simplicity of methods of introduction of fluids into cancellous bone and found that the radiopaque solutions and suspensions which were introduced into cancellous bone in the extremities of the cadaver are rapidly removed into the venous system through regional superficial or deep veins. Their experiments suggested that the venous system of a limb could be filled easily and safely through a needle inserted into cancellous bone at numerous sites. The simplicity and safety of this procedure and the fact that it can be used in edematous limbs in which superficial veins are not visible further justify the clinical application of this technique. The danger of osteomyelitis after transfusion into medullary cavity of infants must, however, be remembered.—*Ralph S. Bromer, M.D.*

Jakob, A. Knöchenveränderungen bei trophischen Störungen am Unterschenkel. (Bone changes in trophic disturbances of the lower extremities.) *Fortschr, a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Jan., 1955, *82*, 28–34.

When one sees periostitis or sclerosis of the bone in the lower extremities, a diagnosis of syphilis or old osteomyelitis is entertained first.

The author has noted the above changes in patients with varices, ulcerated and nonulcerated, in the lower extremities. The bone changes were due to chronic stasis of the blood and lymphatic supply. When an ulcer was present, it was not in the area of the bone changes. The blood Wassermann was negative in all of the patients. Trophic skin changes were present in all cases. The periosteal bone changes were always seen in the fibula and less frequently in the tibia. Two patients with marked sclerosis of os calcis were seen, one subsequent to frost-bite. Histological study of the bone in the latter case showed no endoarteritis. The bone changes here are explained through the slowing of the blood flow.—*Samuel Richman, M.D.*

Carnesale, Peter L., and Guerrieri, A. G. Fibular transplant for loss of substance of tibia; report of a case. *J. Bone & Joint Surg.*, Jan., 1955, *37-A*, 204–206.

In the case reported in this article, the patient was a twenty-seven year old male who had sustained a compound fracture resulting from a gunshot wound, seven years previous to his admission to the hospital. Roentgenograms of the right lower leg showed an absence of the middle third of the tibia and a healed fracture of the fibula with posterior bowing. Sclerotic changes were present in the distal fragment of the tibia. Only on intact fibula had provided stability of the leg.

The distal fragment of the tibia was secured, at a second operation, to the distal portion of the fibula with bone screws and bone chips, and bone chips taken from the ilium were packed about the area through the same incision. At a previous operation, the interval being approximately six and a half months, osteotomy of the upper end of the fibula had been performed and after the contact surfaces had been freshened down to endosteal bone, the fibula was secured to the lateral aspect of the proximal fragment of the tibia with screws. In the interval the extremity had been immobilized in a long cast.

Two years and two months after the second operation, roentgenograms showed union between the tibia and fibula and marked hypertrophy of the transplanted fibula. This procedure was used because the defect in the patient's tibia was large and also because of inadequate skin on the anterior aspect of the patient's leg. Only this procedure was successful after several had failed, including bone-grafting which resulted in infection and deep scarring and required repeated débridements. The authors regard the marked hypertrophy of the transplanted fibula as emphasizing most graphically Wolff's postulate.—*Ralph S. Bromer, M.D.*

Nemethi, Carl E. The primary repair of traumatic digital skeletal losses by phalangeal recession. *J. Bone & Joint Surg.*, Jan., 1955, *37-A*, 78–88.

Phalangeal recession surgery is indicated in those patients demonstrating large soft tissue wound gaps

when an entire phalanx or joint, or both, have been lost and the distal segment of the finger can be salvaged. In order to span the wound gap and to effect a successful repair, there must remain a viable soft tissue bridge containing a functioning artery and nerve (or a reparable nerve), and the soft tissues distal to the wound must be viable. There should also be sufficient bone structure to ensure a greater finger length than would result from amputation. Preservation of the distal phalanx with its highly specialized sensation, especially that of stereognosis, its nail, and general cosmetic value is the aim of the author, together with retaining as much as possible of the over-all length of the digit.

Patients suitable for phalangeal recession should be operated upon within six hours of the time of injury. Complete roentgenographic study should be made. Roentgenograms should demonstrate not only the injured fingers but also the entire hand and wrist. Anteroposterior and lateral views are usually adequate but occasionally oblique projections are necessary. Roentgen examination not only shows the amount of bone remaining, but also furnishes a permanent record of the injury.

The gap is closed by fixing the distal bone fragment to the proximal one with Kirschner wire. The resulting finger is shorter than normal, but demonstrates good motion, sensation and cosmetic appearance. The fundamental functions of the normal hand are better salvaged by phalangeal recession surgery than by amputation.—*Ralph S. Bromer, M.D.*

Jones, G. Blundell. An unusual fracture-dislocation of the carpus. *J. Bone & Joint Surg.*, Feb., 1955, *37-B*, 146–147.

The unusual fracture described in this short report is that of a fracture of the scaphoid of the carpal bones in good position and a fracture of the capitate with the proximal fragment inverted. The patient, a male aged thirty-one, fell 10 feet and, on breaking his fall, injured his wrist. No reduction had been carried out but the injury was thought to have been a transscaphoid, transcapitate perilunar fracture-dislocation of the carpus which underwent spontaneous reduction with inversion of the proximal fragment of the capitate. Owing to the instability of the carpus and the importance of getting union of the scaphoid it was decided to leave the capitate alone until the scaphoid was united. Immobilization in plaster was continued for four months, by which time roentgenograms showed early union of the scaphoid but with evidence of avascular changes in the proximal pole of the capitate.

Further treatment was by active use and exercise. A year after injury, roentgenograms revealed that the proximal fragment of the capitate had united in the inverted position and had regained its normal density. The scaphoid was sound and the calcification of the carpus was good.—*Ralph S. Bromer, M.D.*

Ross, Donald, W., and Vitale, Carmelo C. Monostotic fibrous dysplasia of the metacarpal; a case report. *J. Bone & Joint Surg.*, Jan., 1955, *37-A*, 196–200.

The group of bone lesions known for many years in the literature as osteitis fibrosa has been divided by the students of osseous pathology into several separate and distinct entities. One of these is the solitary bone cyst known as monostotic fibrous dysphasia. This lesion usually occurs at a single site in the metaphyseal end of the long bones of healthy children and is not accompanied by systemic, metabolic, endocrine or other skeletal changes. For these reasons it should not be confused with von Recklinghausen's disease or with Albright's disease. Both of these conditions produce multiple bone lesions. The latter is also known as polyostotic fibrous dysplasia.

The authors report a case of monostotic fibrous dysplasia involving the second metacarpal. In their review of the literature they could find no case report of occurrence in the small bones of the hands and feet.

The patient was an eight year old white boy. Roentgenograms on admission to the hospital showed an expanding lesion of the second metacarpal of the right hand. He had a history of a previous admission when a biopsy was done. The mass as shown in the roentgenogram had a dense, opaque and mottled appearance. An osteotomy was performed and a tibial graft was inserted in the defect. The behavior of the tibial graft was interesting. After two months, the graft appeared in the roentgenograms as a dense shadow with almost parallel sides. The final roentgenogram seemed to indicate that the patient had been provided with a new metacarpal bone. The tibial graft was of both cortical and cancellous type and there remains no doubt, according to the authors, that it was vascularized and replaced by healthy new bone. Since the graft had been seated into the intact periosteal tube of the shaft of the excised bone and had the same muscle attachments, the same stresses and strains may have been exerted upon it as upon the original bone.—*Ralph S. Bromer, M.D.*

Pygott, F. Arachnodactyly (Marfan's syndrome) with a report of two cases. *Brit. J. Radiol.*, Jan., 1955, *28*, 26–29.

Marfan's syndrome comprises multiple developmental abnormalities, one of which, elongation and narrowing of the bones of the feet and hands, gives the condition its alternate designation of arachnodactyly. Other skeletal changes include dolichocephaly or brachycephaly, palatal abnormalities, funnel chest or pigeon breast. There is marked hypotonus and lack of muscular development with resulting hypermobility of the joints. Ectopia of the lens of the eye or iridodonesis is present in 60 to 75 per cent of the cases. Cardiovascular abnormalities are

found in 20 to 30 per cent and are often the immediate cause of death, the commonest abnormality being dissecting aneurysm of the aorta.

Two patients are reported—the first a boy of fourteen with characteristic changes in the hands and feet and thoracic cage and congenital cardiac disease, possibly patent interventricular septal defect with mitral stenosis; the second a woman of forty-four with the typical appearance of the hands and feet and with gross cardiac enlargement and three dissecting aneurysms of the aorta.—*Leslie K. Sycamore, M.D.*

JACK, E. A. Bone anomalies of the tarsus in relation to "peroneal spastic flat foot." *J. Bone & Joint Surg.*, Nov., 1954, *36-B*, 530–542.

Twenty-three cases of tarsal anomaly—talocalcanean bridge or calcaneonavicular bar—occurring among 30 cases of "peroneal spastic flat foot" were studied. Twelve cases had calcaneonavicular bars (9 bilateral and 3 unilateral) and 11 had talocalcanean bridges (3 bilateral and 8 unilateral). Only 7 of the 30 cases presented no evidence of one or the other anomaly. These two anatomical defects have similar developmental cause. In each case the tissue uniting the two main bones may be completely osseous (synostosis) or the bone may be divided by a fissure of varying depth which may consist of cartilage (synchondrosis) or fibrous tissue (syndesmosis). The authors of most earlier articles, according to Jack, quoted from the work of anatomists of fifty years or more ago who described two small accessory bones occasionally found in each situation, the os sustentaculi and the calcaneum secundarium. The tendency has been to consider that the accessory bone lies at the root of the patient's trouble and that its fusion to one or the other, or to both, of the main bones is the cause of the syndesmosis, synchondrosis or synostosis. This view is not entirely in accord with the opinion of the author of this article. The bony processes vary considerably in their nature and dimensions. A calcaneonavicular bar may be a massive structure, well over an inch in width and it may extend across to the medial side of the navicular bone. A talocalcanean bridge may also be wide and it may involve the whole of the sustentaculum facet as well as the area behind it. Fissures may be olique or central and they may not necessarily be confined to one or other extremity of the bony bar. Roentgenographically, only a small proportion of the the anomalies present anything to suggest that they are derived from an accessory bone that has fused on one side or the other.

Bony anomalies of the foot are difficult to detect in the routine anteroposterior and lateral projections of the foot and special oblique views of the foot and axial views of the heel are necessary for diagnosis. One of the roentgenographic features which has been emphasized particularly, is the bone spur which forms on the dorsal and lateral side of the head of the talus. This spur formation is by no means diagnostic of a tarsal anomaly. It occurs in other conditions in which there has been long standing valgus deformity at the midtarsal joint. In the present series of cases spurs were seldom found in the young patients, but became more constant after the age of sixteen. They tend to develop during adolescence in cases with severe persistent symptoms and in older patients with rigid eversion of the foot. They may become large, and in fact, the whole navicular bone may become enlarged so that the naviculocuneiform joints are also spurred. In patients with severe persistent spasm spurs may form not only on the superolateral aspect of the talus, but also on the superolateral aspect of the cuboid and calcaneum.

In regard to symptoms, the author's cases are divided into three categories: In the first are those who complained originally of an acute incident of pain and peroneal spasm which settled permanently after treatment. In the second are those patients who complained of chronic persistent pain and stiffness or who relapsed after an acute incident of spasm. The third category comprises those patients who have anomalies without symptoms. True peroneal spasm, often also involving the extensor digitorum longus, was noted frequently at some stage during the course of observation usually in the younger patients. Eversion of the heel, varying from a minor to a gross degree, was almost the rule. Subtalar mobility is nearly always abolished by a talocalcanean bridge. In the article the symptoms are discussed in detail.

It has been suggested that there should be three categories of the peroneal spastic flat foot. The first would include the bony anomalies talocalcanean bridge and calcaneonavicular bar. The second would include those cases without bone anomaly in which spasm is caused by injury, inflammation or mild infection. The third would embrace those cases seen late as rigid flat foot due to atrophic arthritis and other types of arthritis, old infection etc.—*Ralph S. Bromer, M.D.*

HARRIS, R. I. Rigid valgus foot due to talocalcaneal bridge. *J. Bone & Joint Surg.*, Jan., 1955, *37-A*, 169–183.

This article records the author's further experience with the variety of rigid valgus foot which is due to talocalcanean bridge and calls particular attention to a group of cases in which the anomaly falls short of producing a complete bridge from talus to calcaneus and hence is more difficult to recognize both clinically and roentgenographically. In a previous article (1948) 15 of 17 cases of rigid valgus foot (peroneal spastic flat-foot) were due, not to peroneal spasm, but to congenital fusions of the major tarsal bones. The foot problem with which the author is concerned in this article is due to a congenital bond

between the talus and the calcaneous on their medial surfaces. This anomaly is one of a group, all of which result in stiff and deformed feet. The clinical picture is commonly designated "rigid flat-foot" or "peroneal spastic flat-foot." In the fully developed type of the lesion he discusses in this article, in which a solid bridge of bone unites the talus to the calcaneus, neither of these terms accurately describes the condition since the foot is not always flat, and the peroneal muscles are not always in spasm. The term "rigid valgus foot" is a broader and more widely applicable designation, especially when followed by the name of the anomaly which is its cause.

Roentgen examination is an important agent in the diagnosis of these congenital tarsal fusions. A technique is recommended which displays the talocalcanean bridge when it is complete or nearly complete. In a normal foot a roentgen-ray beam projected from behind, downward and forward, at an angle of 45 degrees or somewhat less, will pass through the plane between the sustentaculum and the neck of the talus, clearly revealing the joint. When a talocalcanean bridge is present, the shadow of its mass obscures the joint. In its place a bony knob is seen. The resulting roentgenogram is distinctive especially when the lesion is unilateral, so that the abnormal foot can be compared with the normal foot. If the anomaly is incomplete, however, it may be difficult to demonstrate its presence by roentgenography.

In addition to the primary lesion, roentgenography can show secondary changes of great significance. Fixation of two major tarsal bones (in this instance the talus and calcaneus) disturbs the complex perfection of movement in the subtalar-mid-tarsal set of joints and results in abnormal binding and cramping of joint surfaces at the extreme of the arc in some planes of movement. This results in osteoarthritic lipping, most conspicuous at the superior margin of the head of the talus. Furthermore, the talocalcanean bridge which binds these two bones together interferes with the development of the articular cartilage of the subtalar joint. This is recognizable in the lateral view by thinning of the joint space. In the lateral roentgenogram there also can be noted the absence of a clear picture of the joint between the sustentaculum tali and the neck of the talus.

It was formerly Harris' opinion that probably all cases of talocalcanean bridge could be visualized by this roentgenographic technique. Even those cases in which the bridge was not quite complete, the narrow gap, being filled by a bond of fibrous tissue or cartilage, still displayed the shadow of an abnormal mass of bone. However, he has encountered several characteristic cases of rigid flat foot which displayed no direct roentgenographic evidence of these congenital fusions. Most of these patients without roentgenographic evidence of a congenital fusion of the tarsal bones, presented the characteristic evidence of secondary osteoarthritic lipping of the superior margin of the head of the talus. This he regarded as evidence that movement at the subtalar joint is limited. It seemed reasonable, therefore, to look for some mechanical interference with the movement of this joint, even though roentgenographic evidence was lacking. Of the two anomalies which are known to cause this secondary point change, calcaneonavicular bar is relatively easy to demostrate by an oblique roentgenogram. The visualization of talocalcanean bridge requires much more careful roentgenographic technique. It seemed possible that these exceptional patients might be suffering from an incomplete talocalcanean bridge so disposed that it could not readily be manifest itself in a roentgenogram. Ten such cases were operated upon and opportunity was had to observe four more cases operated upon by colleagues. So far every case of rigid flat-foot lacking direct roentgenographic evidence of talocalcanean bridge which has been explored has presented the phenomenon of bone blocking, due either to a bony mass springing from the posterior margin of the sustentaculum and impinging upon the body of the talus, or to a lip projecting downward from the body of the talus to overlap the articular margin of the calcaneus. These bone masses were so disposed that they did not obstruct the roentgen-ray beam when projected downward and forward through the plane of the joint between the sustentaculum tali and the neck of the talus. Hence their presence was not directly revealed by the roentgenogram. Thus far no roentgenographic technique has been devised that will reveal this change. In either case the bone mass limits movement by acting as a bone block.

Operative treatment of rigid valgus flat-foot should be limited to the relief of disabling pain and the correction of severe deformity. It should consist in subtalar fusion through a medial approach, supplemented by talonavicular fusion when necessary.

In an addendum to the article a note is made that recently another type of rigid valgus flat-foot came to the author's attention. This consisted in fusion of the posterior end of the talus to the calcaneus apparently by fusion of an os trigonum to both bones.—*Ralph S. Bromer, M.D.*

Leitner, Baldo. The mechanism of total dislocation of the talus. *J. Bone & Joint Surg.*, Jan., 1955, *37-A*, 89–95.

The mechanism of total dislocation of the talus, according to the author, is not well understood and there has been much difference of opinion about it. In his summary, he states that total dislocation of the talus results either from excessive supination or from excessive pronation; accordingly the dislocated talus lies either laterally or medially. A first-degree supination injury results in medial subtalar dis-

location; a second-degree supination injury results in medial subtalar dislocation with talocrural subluxation; and a third-degree supination injury results in total dislocation of the talus.

A first-degree pronation injury results in lateral subtalar dislocation; a second-degree pronation injury results in lateral subtalar dislocation, together with talocrural subluxation; and a third-degree pronation injury results in total medial dislocation of the talus.

The supination mechanism occurs much more frequently than the pronation mechanism. Drawings illustrating the mechanism leading to total dislocation and roentgenographic reproductions showing the types of injury of the author's classification are included in the article.—*Ralph S. Bromer, M.D.*

Gardiner, T. B. Osteochondritis dissecans in three members of one family. *J. Bone & Joint Surg.*, Feb., 1955, *37-B*, 139–141.

Osteochondritis dissecans affecting a single joint is relatively common. Multiple lesions are less common and the occurrence of osteochondritis dissecans in several members of a family was considered sufficiently rare by the author to warrant reporting.

Three cases in two brothers and a sister are described. In the brothers both knees were involved. None of the other joints of the skeleton was affected in any of the patients.

The roentgenograms which are reproduced in the article show the typical changes of osteochrondritis dissecans.—*Ralph S. Bromer, M.D.*

Pick, M. Pickering. Familial osteochondritis dissecans. *J. Bone & Joint Surg.*, Feb., 1955, *37-B*, 142–145.

In this article the occurrence of osteochondritis dissecans involving bilaterally either the knees or elbows of four members of one family is reported. The patients were a mother and three of her four daughters.

The etiology of the condition is unknown. Two hypotheses have been advanced, the traumatic and embolic. In previous reports in the literature of familial occurrence the suggestion of an underlying hereditary or constitutional factor was made. The author thinks that the underlying pathology may be developmental, resulting in a form of localized osteochondrodystrophy.—*Ralph S. Bromer, M.D.*

Sotelo-Ortiz, Frederico. Chronic coccidioidal synovitis of the knee joint. *J. Bone & Joint Surg.*, Jan., 1955, *37-A*, 49–55.

A review of the literature indicated that very little has been written concerning chronic synovitis of coccidioidal origin. This disease may be confused with tuberculosis, particularly in parts of the country where coccidioidomycosis is uncommon. Furthermore, as the result of wartime exposure and rapid modern transportation, it seems probable that it will be seen more frequently in regions where its presence will not be suspected.

The site of primary infection is usually in the lungs, but occasionally the point of entrance is the skin or possibly the tonsils. Primary coccidioiomycosis is an acute, usually benign, pulmonary infection. It is characterized by malaise, anorexia, chills, fever, headache, night sweats and pleurisy. Roentgenograms demonstrate hilar or peribronchial thickening and pneumonitis, and the larger lesions show actual cavitation. The cavities as a rule heal in a few weeks or months, but occasionally persist. Recovery is usually rapid and complete.

A primary infection confers immunity on the host in a manner similar to that produced by a primary tuberculous infection. However, an occasional case may pass into the progressive virulent type, with widespread involvement. In the soft tissues, abscesses are formed which in the paravertebral region become calcified. Any or all organs may be involved with the notable exception of the digestive tract. The bones become infected by direct extension from soft tissue lesions or by hematogenous spread, presenting a picture similar to tuberculous or pyogenic osteomyelitis. The lesions of bone are found only in the disseminated form of the disease. They are primarily destructive, involving bone and cartilage, and are usually multiple. There appears to be a predilection for cancellous bone, as the lesions occur commonly in the vertebral bodies, in the pelvis and in the ends of the long bones. Involvement of the shafts of the long bones does not occur, except by direct extension from adjacent lesions. However, in the short tubular bones such as the phalanges, primary shaft lesions have been noted.

Joint involvement occurs by direct extension through bone and articular cartilage from adjacent lesions. Primary involvement of joints is rare. A special predilection for bony prominences such as the tibial tubercle, the malleoli, the humeral condyles, the olecranon process, and the radial styloid process is characteristic. Narrowing of the joint space occurs when joints are involved, destruction of the joint and ankylosis may follow if the patient survives. In primary joint infections only the synovial membrane may be affected, in which case only capsular thickening or fluid is apparent in the roentgenograms. With progression of the synovial infection, marginal joint destruction, resembling that seen in tuberculous synovitis occurs, followed by destruction of the joint. However, in coccidioidal arthritis, the regional bone atrophy is not as marked in the latter infection.—*Ralph S. Bromer, M.D.*

Blood and Lymph System

Trabucco, Armando, and Márquez, Fernando. The venous junction of the glomerular artery. *J. Urol.*, Dec., 1954, *72*, 1061–1073.

The first part of this article gives a description of the detailed anatomy of the glomerulus and the postglomerular artery. By means of a technique previously reported, the authors inject a black colored latex compound into the venous system and a white latex preparation into the arterial system. In this way the filling of an entire renal circulatory system is completed; the organic material is then digested. This technique is based upon the premise that under carefully controlled uniform pressures of 2 to 4 cm. of mercury there will be no reflux of the black dye into the arterial system from the venous injection.

Two main types of postglomerular artery are described. The first group is composed of those vessels which form a very extensive arterial capillary network before entering the veins. The second group has a more or less direct communication between the postglomerular artery and the vein. Various subgroups of each large group are also described. There are twenty illustrations showing the above noted anatomical formations.

The second part of the article is concerned with a discussion of renal physiology on the basis of the two types of postglomerular arteries.

When the capillary network of arteries is interposed between the glomerulus and the vein, these vessels are in close proximity to the renal tubules in such a manner that a sanguineous lacuna is produced. Contraction of the postglomerular portion of the arteries causes blood to flow through the glomerulus, hence filtration occurs into Bowman's capsule. With relaxation of the postglomerular artery, changes in osmotic tension produce resorption from the tubular system into the network of vessels. The changes in osmotic tension are associated with hemoconcentration following the filtration of material through the glomerular portion. Thus, in one portion of the system, the variations in osmotic pressure produce transfer of certain elements from the blood into the tubular system, whereas, in another portion of this complex system, there is resorption of some of the materials by the cells of the tubules so that physiological processes are carried out. It has been shown anatomically that some of the arterial capillary systems open directly into large venous trunks. The latter may behave in a suction-like manner helping to drive the blood that is in the adjacent capillary lacuna. This theory indicates that the work of excretion and absorption is entirely arterial.

The postglomerular arteries which directly join the veins are supposedly a defense mechanism against pathological injuries. They are more numerous in the juxtamedullary portion of the kidney and there is no interposition of a capillary network. Many of the glomeruli of these vessels are quite small but are functioning glomeruli. There is in essence, however, a direct communication between artery and vein in these instances. The uriniferous tubules of the glomeruli associated with these vessels may be filtered by other capillaries of the network system. If injury occurs in the capillary lacuna, the renal economy is preserved because of the blood flow through the direct arteriovenous communications.—*George W. Chamberlin, M.D.*

Epstein, A. A., and Cole, L. J. Hyperplasia of Brunner's glands. *J. Canad. A. Radiologists*, Dec., 1954, *5*, 43–45.

Only 3 cases of hyperplasia of Brunner's glands have been reported in the literature up to 1953. The authors describe in detail a similar case, in which the diagnosis was made on the basis of roentgen examination.

Roentgen studies of a fifty-two year old white male revealed a normal gallbladder. The gastrointestinal series disclosed a polypoid appearance of the duodenal caput.

The roentgen characteristics were multiple, sharply defined filling defects within the duodenal bulb and extending into the descending limb. These defects were largest and most abundant in the bulb, and presented a typical "Swiss cheese" pattern. No evidence of ulceration was noted.

The patient underwent abdominal exploration. At operation the pertinent findings were confined to the first portion of the duodenum. Duodenotomy and gastrotomy showed the duodenal mucosa to be heaped up and to almost obliterate the duodenal lumen. This opening was closed and an anterior gastroenterostomy and abdominal vagotomy were carried out.

A number of sections of the specimen from the duodenum were made and examined. This specimen was seen to be made up of numerous lobules of typical Brunner's glands. These lobules were separated from each other by thin strands of fibrous connective tissue. No evidence of malignancy was found.

These glands are most numerous in the first part of the duodenum and become less frequent and finally disappear in its more distal parts. They may, however, extend into the pylorus for a short distance. They have been observed, on occasion, in the first part of the jejunum. The function of these glands appears to be to produce extra mucus at the site where the pancreatic enzymes are emptied into the intestine. This presumably may have a protective effect in cases of hyperacidity.

In the differential diagnosis the following must be considered:

1. *Benign intraluminal neoplasms of the duodenum* produce usually a solitary rounded or lobulated de-

fect. Multiple radiolucencies may be found occasionally due to adenomatous polyps and very rarely to hemangiomas or lipomas. The roentgen demonstration of pedicles and the presence of polyps in other portions of the small intestine, or concomitant gastric polyposis will help to distinguish duodenal mucosal polyps from hypertrophied Brunner's glands.

2. *Duodenitis* under certain circumstances can simulate gandular hyperplasia. The characteristic features are: (a) bulbar irritability, with or without spastic deformity; (b) inconstancy in size, shape and position of the defects; (c) obliteration of the radiolucent shadows by compression.

All of the above criteria are not present under therapy in hyperplasia.—*Stephen N. Tager, M.D.*

Healy, Romeyn, J., Amory, Harold, I. and Friedman, Milton. Hodgkin's disease; a review of two hundred and sixteen cases. *Radiology*, Jan., 1955, *64*, 51–55.

The authors support the theory that Hodgkin's disease is unicentric in origin. Early diagnosis by means of biopsy of lymph nodes is urged. Indications for lymph node biopsy are: (a) an enlarged lymph node, chiefly in the lower cervical chain; (b) persistence of the enlargement for three weeks or longer; (c) absence of a regional inflammatory lesion as a cause for the adenopathy. The disease is classified as Stage I, II, or III, depending upon the extent of lymph node involvement.

The primary treatment of Hodgkin's disease should be aggressive roentgen irradiation. The authors suggest dosages of 1,500 r in one week, up to 2,500 r in three weeks; for some of the more resistant lesions, a total tumor dose up to 4,000 r is given. They apply this principle to all stages of the disease.

Tables are presented comparing their survival rates with those of other authors. In their series of 216 cases of Hodgkin's disease, the absolute five year survival rate was 37 per cent.—*E. E. Seedorf, M.D.*

Lynn, R. B., Steiner, R. E., and Van Wyk, F. A. K. Arteriographic appearances of the digital arteries of the hands in Raynaud's disease. *Lancet*, March 5, 1955, *1*, 471–474. (From: Departments of Radiology and Surgery, Postgraduate Medical School of London, Hammersmith Hospital, London, England.)

Twenty-three patients with ages ranging from fifteen to sixty-five years who had intermittent spasm and color changes of the fingers were studied by arteriography. The method used is briefly described. Two distinct groups of patients were found: (1) Those who have had intermittent spasm of the digital arteries without any anatomical abnormalities, and (2) those with obliteration of the digital arteries. The former very rarely develop nutritional changes, while the latter frequently do.

The authors propose that the term "Raynaud's disease" is more appropriate for the first group of patients and "thrombotic digital artery disease" for the second group.—*P. B. Parsons, M.D.*

Reggianini, Valerio, and Bono, Carlo. La sindrome da ostruzione venosa del'arto superiore. (Syndrome of venous obstruction of the upper extremity.) *Ann. ital. di chir.*, 1954, *31*, 863–881. (From: Clinica Chirurgica dell'Università, Bologna, Italy.)

This condition is sometimes referred to as the Paget-Schroetter syndrome, named after its discoverers. Its etiology and pathology remain somewhat obscure. It is still a rare entity and Hughes was able to collect only 320 cases from the literature in 1949.

Although it may occur at any age, it is most common in early and middle aged people and most often in men. The onset is usually sudden following either trauma, severe strain or brisk movement of the arm. The symptoms are pain of the arm and shoulder associated with edema and cyanosis of the affected limb. Rarely does paresthesia or paralysis develop. Later the superficial veins of the arm and shoulder become prominent. Symptoms may last from a few weeks to several months, depending on how well the collateral circulation develops. No one today has been able to show that in cases of venous thrombosis either absorption of the thrombus or recanalization of the vein takes place.

The diagnosis presents no particular problem. The condition may rarely be confused with aneurysms of the ascending arch of the aorta, mediastinal tumors, metastatic lymph nodes and bronchogenic carcinoma.

Although the symptoms and physical findings point to a stasis or obstruction of the axillary or subclavian vein, there is nothing to suggest underlying pathology.

The authors report 8 cases of venous obstruction of the upper extremity. In 5 of 6 cases studied with venous injection alterations of the major veins were present. However, although this procedure may show the points of obstruction or constriction of the vein or it may visualize the collateral veins of the arm and shoulder, very little information is gained as regards the underlying cause. In only 1 case treated by surgical intervention could a diagnosis of thrombus be confirmed. In the other cases venous thrombophlebitis was thought to be the most logical clinical diagnosis and therapy was instituted on this basis.

Complications are infrequent and usually are the result of pulmonary embolism. This has rarely led to death in the cases reported.

Other causes which may be considered in the eti-

ology of this condition are pinching of the vein between two bony structures such as the clavicle and first rib, tearing off of smaller tributary veins, spasm of the vein, etc.

These cases usually do well with conservative treatment and the use of anticoagulants. The duration of the disease is shortened and the normal function of the arm returns in most instances. Although phlebectomy would appear to be the treatment of choice, it is uncertain whether a thrombus will be found and besides such intervention increases the risk of pulmonary embolism. Sympathectomy has also been used based on the theory of venous spasm. This latter, however, has not produced as good results as those obtained by conservative treatment or phlebectomy. The use of anticoagulauts allows recanalization of the afflicted vein.—*Peter E. Russo, M.D.*

Sutton, David. Percutaneous angiography with special reference to peripheral vessels. *Brit. J. Radiol.*, Jan., 1955, *28*, 13–25.

Two hundred and fifty cases are analyzed in which percutaneous angiography has been used or the investigation of the peripheral vessels of the limbs, the majority involving the lower extremity. Angiography of the upper limb was performed thirty times by puncture of the subclavian or brachial artery. The brachial artery is usually entered opposite the lower third of the humerus. The congenital anomaly of high bifurcation of the brachial artery may complicate puncture at this site. Care must be taken to avoid too much local trauma since the artery is prone to spasm and cases are on record in which occlusion has occurred with subsequent amputation. Thirty-five per cent diodone is used for the injection.

Puncture of the femoral artery is simple but the popliteal artery presents more difficulty. A preferable procedure is catheterization of the femoral artery down to the popliteal fossa. Forty-two per cent diodone is usually used in the femoral artery.

Lesions investigated in the series included acute embolic occlusion, aneurysm, angioma, and obliterative vascular disease, with the latter category comprising by far the largest number of cases. The roentgenologic diagnosis of atheromatous peripheral vascular disease by angiography is straight-forward. In the lower extremity the maximal incidence is at the lower end of the femoral artery just about or above the opening of the adductor canal. Most occlusions appear to commence at this point and may extend upwards or downwards. In some instances symptoms of impaired circulation occur in the lower extremity from occlusion of the aorta or iliac artery. Such cases may require both lumbar aortography and femoral arteriography.

Although the diagnosis of atheromatous vascular disease can usually be made with high accuracy on clinical ground alone, in young individuals the picture may not be clear clinically and arteriography may be invaluable in establishing the diagnosis. Furthermore, with the development of the surgical treatment of occlusive vascular disease, the exact localization of the involved area by arteriography is essential.

Cases of peripheral vascular disease not due to atheroma such as thromboangiitis obliterans, juvenile obliterative arteritis, endarteritis obliterans and peripheral arterial occlusion associated with diabetes cannot be differentiated by arteriography. The angiogram usually shows normal vessels as far as the ankle with evidence of occlusion below this point. Since femoral injection frequently results in poor visualization of the vessels of the foot, injection is best performed at the level of the popliteal fossa.

In addition to the cases of vascular disease 26 cases of suspected tumors were investigated. The main value of the angiogram in these conditions appears to be in providing positive evidence of the presence of a malignant tumor by the demonstration of pathological vessels and increased vascularity. In the case of metastatic lesions some clue may be obtained as to the primary source.—*Leslie K. Sycamore, M.D.*

General

King, Geraldine, and Schwarz, Gabriel A. Sturge-Weber syndrome (encephalotrigeminal angiomatosis). *A.M.A. Arch. Int. Med.*, Nov., 1954, *94*, 743–758.

The classic clinical manifestations of the Sturge-Weber syndrome or encephalotrigeminal angiomatosis include a vascular nevus of the face, a hemiplegia contralateral to the cutaneous lesion, an intravertebral calcification, various abnormalities of the ipsilateral eyeball, convulsive seizures, and mental retardation. W. Allen Sturge described the first case in 1879. He also described, much later, the intracerebral calcifications. The calcifications are deposits in the cerebral cortex and not due to calcified blood vessels in the leptomeningeal angioma.

Besides the vascular malformation, which is considered to be the underlying defect, marked alterations in the structure of the cerebral cortex, especially of the occipital lobe, are recorded. The affected cortex is hard, atrophic and shrunken. This is probably due to deposition of large amounts of iron and calcium in the vessel walls of the cortex and later in the interstitial substance as well.

The basis of the disease is considered to be an embryonal defect and a discussion of the embryology is given.

Five cases are reported with several variations of the disease, that is not all having the classic signs and symptoms of the disease. A heretofore undescribed finding was an associated calcified subdural hematoma in a patient with the Sturge-Weber syn-

drome. The most persistent findings in the authors' cases were facial nevi, focal seizures, electroencephalographic changes and ocular abnormalities.

Surgical and roentgen or radium therapy have been advocated in treatment. The authors feel the more radical surgical procedures should not be done unless anticonvulsant therapy has been a total failure.—*Lawrence A. Pilla, M.D.*

Carroll, Robert E., Sinton, William, and Garcia, Alexander. Acute calcium deposits in the hand. *J.A.M.A.*, Jan. 29, 1955, *157*, 422–426.

The authors, who are from the New York Orthopedic Hospital, give a very clear and interesting presentation of acute calcium deposits in the hand. They emphasize that this condition is a great deal more common than has been previously appreciated. Their study is based upon 100 consecutive cases. The largest previously reported series consisted of 15 cases.

Clinically, the abnormality is manifested by the onset of sudden, acute, severe pain which brings the patient quickly in search of medical attention. The area was swollen in 85 per cent of cases, marked localized tenderness was present and in four-fifths of the cases studied there was local redness. The youngest patient was thirteen years of age and the oldest was eighty-one. The authors present a composite diagram of the hand indicating the locations of the calcium deposits which were demonstrated roentgenologically. The most common site is in the tendon of the flexor carpi ulnaris near the pisiform. The deposit was in this location in 37 of the cases. Calcium deposits were also found commonly in the long digital flexors and extensors, in the supporting ligaments of the digits, in the palm of the hand and in the short intrinsic muscles and tendons.

The pathogenesis is believed to be essentially the same as that in the shoulder. Local necrosis of tissue presumably causes deposition of calcium salts, perhaps through the intermediary stage of a soap or fatty acid.

The disease is acute, severe and self limited. When no treatment was administered, the symptoms persisted an average of twenty days. Hot soaks decreased the duration to twelve days. Local injection with procaine gave immediate relief from pain while complete relief required an average of six days. The authors prefer local procaine injection followed by soaking of the hand in warm water. Roentgen therapy is not mentioned. Usually the calcium deposits disappear at about the same time as the symptoms are relieved. The average disappearance time for calcium deposits was fourteen days. The authors state that, in essence, the deposit is a chemical furuncle which is absorbed, ruptured spontaneously or is lanced by the physician's needle.—*C. L. Hinkel, M.D.*

RADIATION THERAPY

Arnold, Arthur, Bailey, Percival, Harvey, Roger A., and Haas, L. L. The application of the betatron to the treatment of brain tumors; studies of high energy irradiation of brain tumors provided by the betatron seem to point to better results than by treatment with the conventional x-ray. *South. M. J.*, Jan., 1955, *48*, 63–67.

Coventional radiation therapy leaves much to be desired in the treatment of malignant central nervous system tumors since it offers only a few weeks to a few months palliation. With the betatron, which has a peak energy of 23 mev., a more uniform and effective tumor dose delivered with multiple field technics has resulted in longer survivals and improved palliation in 60 per cent of the cases treated. The principal physical advantages of this high energy beam are three-fold: (1) greater penetration, (2) freedom from side-scatter, and (3) insignificant surface dose with maximum reaction at about 4 cm. depth.

It is well recognized that there is no significant known qualitative difference between high energy roentgen rays and conventional roentgen rays but there is a definite quantitative difference in the biological effect produced, with those of high energy having less effectiveness per unit dose. Further studies will be necessary to evaluate a possible specific selectivity of effect on malignant cells.

From observations on monkey brains as well as on the brains of patients, it was noted that the tissues of the central nervous system are much more radioresponsive than previously thought. The primate brain stem has proved to be the most radiosensitive area of the brain while the cerebral cortex is relatively resistant. Late necrosis may occur as long as a year after treatment and is best managed by surgical excision of the necrotic tissue. These findings determine the upper limits of tumor dose tolerated in each location.

All clinical, radiologic, and surgical data must be utilized in accurately planning the treatment with close cooperation between the surgeon and radiotherapist. Tumor doses were initially from 5,500–6,500 r, delivered in seventeen to twenty-one days. This was later changed to a tumor dose of 7,500 r in twenty six to thirty days, using the 23 mev. medical betatron in both instances.

The authors state that 22 of their first 25 cases exhibited a favorable response to high energy radiation. Sixteen of these cases had malignant lesions while 9 had benign lesions. These cases are numerically represented as to times of survival, incidence of pathological types, and comparisons with other results.—*K. L. Krabbenhoft, M.D.*

Rohrschneider, W. Strahlenschädigung und Strahlenschutz am Auge. (Radiation injury

and radiation protection of the eye.) *München. med. Wchnschr.*, Jan. 14, 1955, *97*, 33–37.

The visible light rays of the sun and of artificial light sources are not the only rays to which the human organism is exposed. The visible light rays represent only a small part of the electromagnetic spectrum. At the long wave side of the visible light rays follow the infrared rays, the micro-waves, the ultrashort waves and short waves, the radio waves and the long waves of the high frequency rays. At the opposite side of the visible light rays follow the ultraviolet rays, the X-rays, the gamma rays, and the cosmic rays. All these rays of the electromagnetic spectrum, under natural or artificial conditions, are able to damage the eye.

A sketch is included showing schematically how different parts of the eye are affected by rays of different wave length. The resulting injury is as follows: (1) retinitis by visible light rays; (2) occupational cataract of glassblowers by infrared rays; (3) cataract by micro-waves; (4) snow blindness by ultraviolet rays; (5) cataract by x-rays and gamma rays.

Although the glare blindness which may be harmful to the car driver at night is not a permanent injury of the eye but represents a reversible effect, it is also discussed in the article. As a protection against the blinding rays of the oncoming car the "Gradal-glasses" of Zeiss are recommended. These tinted glasses with an increased absorption of the visible light rays up to 90 per cent toward the upper part of the glasses give protection against the glare blindness by downward flexion of the head. The most darkened upper parts of the glasses come in front of the pupil so that the eye is hit only by a small percentage of the visible light rays. When the oncoming car has passed the head is brought back in normal position, and there is immediately undisturbed vision. As another device the polaroid glasses are mentioned. Their protection is very limited. These glasses absorb only the polarized light rays which are reflected from the wet highway or street pavement. Scotoma of the retina is common after a solar eclipse. Protection against this injury is easily provided by glasses which reduce the light energy and absorb also the infrared rays. A dark photographic plate is a sufficient protection on direct observation of the sun.

The occupational cataract of glassblowers and metal workers represents an injury of the eye produced by the penetrating infrared rays. An effective protection is given by ferric oxide glasses which absorb the infrared radiation.

Ultraviolet rays of the sun especially on glaciers or ultraviolet rays of artificial sun lamps produce the so-called "snow blindness." This snow blindness which persists even for hours after the incident are produced by an overdose of ultraviolet rays and visible light rays in addition. Protection is provided by glasses which absorb the ultraviolet rays as well as a considerable percentage of the vi ible light rays. Such protective glasses are available on the market. The form of these glasses is such that rays coming from the sides and hitting the eye tangentially are also absorbed.

So far, no occupational roentgen cataract in a physician has been observed, only one case in a physicist. Cases of roentgen cataract have been noted, however, as side effects of roentgen therapy of the eye itself or parts of the body close to the eye. These side effects can be avoided by the direction of the Roentgen-ray beam so that no rays at all or only a small percentage hit the eye, and by protection of the eye by lead glass or silver-plated lead eye shields. Numerous persons were seen after the explosion of the atomic bombs in Hiroshima and Nagasaki who after an interval of from six months to 2½ years developed typical radiation cataracts. It is still uncertain whether the injury in these cases was caused by gamma-rays or by neutrons.

Damage of the eye by short wave diathermy has not been observed. The effective agent of ultrashort waves and of micro-waves as produced by radar is again the infrared heat waves which damage the superficial as well as the deeper parts of the eye. The danger of micro-waves is lessened by the pain which develops immediately and serves as a warning signal.

There are two laws of the radiation effect and of the radiation injury: (1) a radiation can be effective and in an overdose damaging only where there is absorption by the tissues; (2) radiation injury can develop only where cells and tissues are sensitive to the respective radiation energy.—*Hans Lewin, M.D.*

Berman, Harry L. Radical surgery after intensive irradiation. *A.M.A. Arch. Surg.*, Nov., 1954, *69*, 603–606.

The evaluation of postoperative complications in surgery following intensive irradiation requires a careful consideration and chronological correlation of radiation dosage, its distribution in affected tissues, and tissue reactions with the course of events before one can conclude that such changes are due primarily to the irradiation or the operation.

The favorable criteria for surgery in previously irradiated tissue include small doses of radiation, small fields of treatment, a reasonable long period of elapsed time between the end of the therapy and the date of the operation, and irradiation with higher voltages. The ability of the previously irradiated tissue to tolerate further trauma before surgery should be considered. Also the time intensity relationship must be considered.

The assumption that irradiation is responsible for all complications following surgery is unwarranted for it often renders surgery more feasible.

The surgeon and radiation therapist must cooperate to provide important information about the spread of various tumors, and consult one another

before surgery is performed on any person having previous irradiation to the site to be involved in surgery.—*J. F. Berry, M.D.*

Fuchs, G., and Lassmann, G. Zur Röntgentherapie der chronischen Thrombophlebitis. (Roentgen therapy of chronic thrombophlebitis.) *Wien. klin. Wchnschr.*, Dec., 1954, *66*, 957–959.

The authors divide the involved extremity into five to six fields and give a daily dose of 15–80 r to one field. The total dose per field is between 100 and 200 r, the total number of treatments amounting from three to fifteen. The technical factors are 150 kv. and 5 mm. aluminum filtration.

Of a total of 25 cases reported, 19 had no recurrence, 2 died from other causes and 3 failed to report. Only 1 case suffered recurrences along with increasing cardiac decompensation and recurrent enteritis. —*Frederick M. Reis, M.D.*

Friedman, Milton, Hine, Gerald, J., and Dresner, Joseph. Principles of supervoltage (2 million volts) rotation therapy; illustrated by the treatment of a chordoma of the vertebra. *Radiology*, Jan., 1955, *64*, 1–16.

The goal of any technique of radiation therapy is to produce rather homogeneous dose distribution within a tumor region with minimal irradiation of the surrounding tissues. The technique used by the authors consists of supervoltage rotation therapy with 2 mev. roentgen rays and the principles and special advantages of this technique are illustrated by the report of a case of a chordoma of the body of the fourth lumbar vertebra.

A large tumor-lethal dose of 7,200 r was delivered in forty-seven days to a cylindrical volume of tissue measuring 6 cm. in diameter and 6 cm. high, which encompassed the tumor. About 3,800 to 4,400 r was the dose received by the spinal cord. A 2 million volt resonant transformer generator was used with 4 mm. of lead filtration which, with a 125 cm. target-tumor distance, produced a roentgen flux of 70 r/min. at the axis of rotation. Treatment times of six to ten minutes delivered a tumor dose of approximately 200 to 350 r per treatment.

Studies of dose distributions in rotation therapy with 200 kv., 2 mev. and 22 mev. roentgen rays were made where the dose at the center of the tumor was the same for all these energies. Using small, 3 cm. diameter fields, the dose distribution is practically the same as with 22 mev. roentgen rays in the high dosage region within the tumor as well as the low dosage region outside the tumor area. The volume dose outside the tumor is twice as high with 200 kv. roentgen rays. With large fields, the dose to the surrounding normal tissues is reduced as the voltage rises from 2 to 22 mev.

By comparing the central tumor dose with the skin dose the relative efficiency of 200 kv. rotation therapy and 2,000 kv. rotation therapy can be compared. In the illustrated case where a 6 cm. diameter field size was employed, the ratio for 200 kv. roentgen rays was 2:1, whereas with 2,000 kv. it was approximately 8:1. This means that with 200 kv. roentgen rays a tumor dose of 7,000 r would give a skin dose of 3,500 r with resulting severe erythema. With 2,000 kv. roentgen rays, however, the skin dose would only be about 900 r. The volume dose to the tissues between the skin and tumor would also be less with the higher energy.

With small field sizes, the irradiated volume is small and rotation supervoltage therapy is most efficient. With increasing field sizes, the volume irradiated increases and the superiority of this technique over the multiple portal technique is reduced.

The rotating platform used rigidly immobilizes the patient in either the standing or sitting position. Precise alignment of the roentgen-ray beam and the axis of rotation with the center of the tumor is required to prevent treatment errors. The steps in localizing the tumor and orientating it with respect to a fixed point on the skin are described. The depth of the tumor from the skin is determined with the aid of a contour device. Following this treatment planning the tumor dose is calculated by graphical summation, wherein the cross section is divided into 12 equal sectors by lines which intersect at the centers of the tumor and the percentage tumor dose for each sector is obtained from appropriate charts. These doses are averaged and the figure obtained represents the tumor dose (with backscatter) in per cent of the air dose at the axis of rotation. The positioning of the tumor at the center of rotation using the right-angle coordinate system is described in detail.

Supervoltage rotation therapy also offers advantages for certain tumors near the skin. Full 360° rotation when the cross section area is small or segmental rotation through 90 to 270° arcs can be used. Carcinoma of the antrum and tonsil and a liposarcoma of the buttock have been successfully treated.—*Donald N. Dysart, M.D.*

Braestrup, C. B., and Mooney, R. T. Physical aspects of rotating telecobalt equipment. *Radiology*, Jan., 1955, *64*, 17–28.

The results of a study of dose distribution and protection requirements of a rotating telecobalt unit are reported. The beam orientation system of this unit differs fundamentally from that of the conventional stationary type units in that the source of radiation is able to move on the surface of a hypothetical sphere, with the useful beam always directed at the center. The basic factors of this equipment are:

Diameter of cobalt source	2.5 cm.
Source-diaphragm distance	30 and 40 cm.
Radius of rotation	75 cm.

Maximum field diameter at axis 23 cm.
Dose rate, in air, at 75 cm. 33 r/min.
Dose rate, in air, at 100 cm. 19 r/min. } (June, 1953)

Good agreement was obtained in the water phantom measurements with the earlier work of other investigators—better than that usually obtained with high energy roentgen rays. A constant dose rate and the nearly mono-energetic gamma radiation permit this. Because of the large diameter of the energy source, a relatively large penumbra is found with short source-diaphragm distances, so therefore longer source-diaphragm distances are desirable. In order to minimize electron contamination, the diaphragm should be 20 cm. or more from the skin of the patient.

Many tables and figures are provided showing the depth doses, isodose pattern and dose determination for this source. With a moving source of radiation it has been found more practical to express tissue dose in terms of the dose at the center of rotation rather than in percentage of the surface dose. This center dose depends solely on the attenuation of the rays, and for a given field size, on the radial thickness of tissue through which the beam has to pass. The dose rate at the center is essentially the same whether the phantom surface is curved or flat and at right angle to the beam. Scales have been made which give directly the center dose for different tissue thicknesses. The contour of the patient is divided into 12 sectors by drawing radial lines every 30°. The scale superimposed on this contour permits reading off directly the contribution of each radial beam to the center dose, following which the average value is computed in the conventional manner.

The off-center dose rate is determined by use of isodose curves which are plotted in percentage of the center dose. Isodose patterns obtained with different size cross sections reveal that the dimensions of the patient have only a minor effect on the relative dose distribution for the same part of the body. Field size, location of the center of rotation, and degree of scanning, on the other hand all produce a significant effect.

Leakage radiation from the source while the shutter was closed varied from 0.3 mr/hr. to 16 mr/hr. at 1 meter in the old source housing. The new source housing provided greater protection and fully met the requirements of the National Bureau of Standards Handbook 54 which state that "the housing and collimating devices shall be so constructed that at 1 meter in any direction from the source in the 'off' position the maximum and average dose rate do not exceed 10 mr/hr. and 2 mr/hr. respectively." The shielding requirements of the room are limited to scattered rays only since the counterweight shield attenuates the useful beam. About half of the scattered radiation comes from the collimating diaphragm.

The authors, in conclusion, compare cobalt 60 teletherapy with supervoltage radiation.—*Donald N. Dysart, M.D.*

Haas, L. L., Wakerlin, R. C., and Destro, V. P. Three-dimensional body forms for use in treatment planning with the 23-Mev betatron, *Radiology*, Jan., 1954, *64*, 105–111.

Treatment of patients with the 23 mev. betatron requires careful planning regarding: (a) accurate tumor localization; (b) field selection, and (c) dose calculation and determination. Rigid masks and body forms are a part of this treatment planning.

Many different materials and techniques were tried in the attempt to find one that was most practical. Direct molding of "Gypsona" or similar plaster bandages on the patient proved to be the simplest procedure for delineation of body perimeters and for preparation of head and other body masks.

These forms have proved to be useful for treatment planning and also for replacement on the patient's body for localization and identification of the selected fields.—*Donald N. Dysart, M.D.*

Santos, Carlos. Lisbon, Portugal. Gezielte scharf lokalisierte Röntgentherapie. (Aimed, sharply localized roentgen therapy.) *Strahlentherapie*, Jan., 1955, *96*, 47–63.

By exact aiming and localization of the roentgen-ray beam, irradiation of the sella turcica alone, of the anterior *or* posterior pituitary lobe, or of selected small volumes of the midbrain is possible. The patient's head is fixed with rice bags and wooden wedges in the "microlocalization" device. With the aid of lead markers arranged like a clock's face superimposed on the device and a film exposed with the therapy tube, the area to be irradiated can be delimited in terms of the circumferentially arranged lead markers, These limits are then set off with lead shields and the radiation administered. As a double check, another film is exposed at the end of each treatment to assure that the dose was indeed administered to the precisely localized area at which it was aimed in the beginning.

Depth dose measurements were made by comparing dental films exposed at the skin level and then for varying periods of time at varying depths with the "roentgen puncture" beam, 5 by 5 mm. in cross section. For practical purposes these measurements gave (with 260 kv., 18 ma., 0.2 mm. Thoraeus filter, and 80 cm. focus skin distance) for each 100 r delivered to the skin 25–30 r at the sella turcica and at the same depth but at a distance of 3 mm. from the edge of the primary beam, 2–3 r.

The indications for this sort of therapy are many, *e.g.*, pituitary tumors; such endocrine abnormalities as gigantism, climacteric disturbances, amenorrhea and diabetes insipidus, rheumatism and its asso-

ciated symptoms; sphenoid and posterior ethmoid sinus infections.

Excellent illustrations make the technique of microlocalization of treatment beams self-evident. Clinical results are given in the form of several reports of patients with diabetes insipidus (in one of whom the improvement following roentgen treatment of the posterior lobe of the pituitary gland is striking) as well as general clinical impressions after one to two years' experience.—*Henry G. Moehring, M.D.*

Bohlig, H. Ergebnisse der Strahlenbehandlung des Brustkrebses in der Zeit von 1922 bis 1948. (Results of radiation therapy of cancer of the breast from 1922 to 1948.) *Strahlentherapie*, Jan., 1955, *96*, 64–74. (From: Strahlenklinik am Stadtkrankenhaus Johannstadt, Dresden, East Germany.)

Of 687 patients with carcinoma of the breast treated between 1922 and 1948, 28 per cent were five year survivals and 21 per cent were alive without evidence of carcinoma at the end of five years. Difficulties due to World War II contributed to lowering these figures both by making therapy of any sort more uncertain and also by causing loss of records.

Of the 203 patients treated from 1946–1948, 33 per cent are symptom-free at the end of five years. This improvement in results is explicable on the basis that war-time difficulties no longer entered and that postoperative radiation dosage has been increased.

The author comes to several conclusions: that the survival rate in breast carcinoma is increased by decreasing the time interval between the appearance of symptoms or findings and definitive treatment; that the survival rate is increased by shortening the time between surgical and postoperative radiation therapy; and that the prognosis is appreciably better in the more differentiated types of carcinoma—adenocarcinoma, solid, or mucin-producing carcinoma. Though his experience with hormone therapy is limited, his results are reported as favorable. He has used radiation castration of younger women consistently only since 1949, so that factor does not enter into the series reported. Preoperative irradiation was used so infrequently that it is of no moment to this report.—*Henry G. Moehring, M.D.*

Skrimshire, J. F. P. Radiotherapy of Cushing's syndrome. *Lancet*, Feb. 5, 1955, *1*, 270–272. (From: St. Thomas's Hospital, London, England.)

Because the signs and symptoms of Cushing's syndrome are caused by adrenal cortical overactivity, it can be controlled by either total or subtotal removal of the adrenal glands, or by reducing the adrenocorticotrophic activity of the pituitary gland by irradiation. The author believes that roentgen control is preferable if adrenal tumor can be excluded. If irradiation fails, surgery can be used later.

Treatment by the author consists of irradiation of the pituitary gland through 6 circular fields with 250 kv., a half-value layer of 1.75 mm. Cu, at 50 cm., to give 4,000 to 5,000 r to the pituitary in twenty-eight to thirty days.

The histories of 6 cases, all women, are presented. One died of cerebral hemorrhage, 1 showed no progression of the disease, and 4 showed remissions. Improvement usually became apparent one to three months after therapy. Plethora and striae slowly cleared, menstruation recurred (although in 2 patients it was irregular), glucose tolerance curves showed improvement (if they were previously abnormal), blood pressure was reduced, urinary corticosteroids diminished in 4 and urinary excretion of 17-keto-steroids was reduced in 2 patients. Hirsutism showed little or no change.

The presence of adrenal tumor may be suspected if the history is short and there are marked changes in the sexual sphere. In men, marked feminizing changes are almost always associated with tumor. Roentgenographic study may demonstrate a tumor with or without the use of a contrast medium.

The prognosis is serious, 50 per cent of such patients dying in five years. Evaluation of therapy is difficult because of normal spontaneous remissions.—*Henry J. Klos, M.D.*

RADIOISOTOPES

Quimby, Edith H. Radioactive isotopes as aids in medical diagnosis. *New England J. Med.*, Jan. 6, 1955, *252*, 1–9.

This article is the George Holmes Lecture before the New England Roentgen Ray Society. Several principles for the diagnostic use of radioisotopes are presented, with examples. These are:

(1) Isotope dilution for plasma volume and red cell mass determinations (iodinated human serum albumin).

(2) Rate of change of isotope concentration in the vascular system as an aid to assess cardiovascular dynamics (radiosodium).

(3) Disappearance rate from a site of injection as an index of local circulation (radiosodium), and

(4) Isotope concentration in specific organs as an estimate of function (radioiodine).

While no new data are given, this article is a clear and interesting summary of some of the important clinical uses of isotopes at this time.—*R. Kenneth Loeffler, M.D.*

Wormall, A. The use of radioactive isotopes in immunology. *Brit. J. Radiol.*, Jan., 1955, *28*, 33–38.

The methods of labelling antigens and antibodies

with radioactive isotopes are described and a number of problems to which these are applicable are briefly reviewed and discussed. The respective merits of four procedures for labelling by isotopes (I^{131}, P^{32}, S^{35} and C^{14}) are considered:

1. Chemical synthesis is impracticable for proteins.

2. Exchange methods involve drastic treatment and the probability of unstable labelling.

3. Iodination, phosphorylation, coupling, etc., is generally the method of choice. The introduction of I^{131} into the 3:5-diiodotyrosine groups by iodination and of S^{35} by the reaction of mustard gas sulphone with the free amino groups both give stable structures but the phosphate groups formed by phosphory chloride are not firmly bound. Double labelling of the same protein with I^{131} and S^{35} has many advantages.

4. Biological labelling enables suitable isotopes to be introduced into the desired material, antibodies, phosphoproteins, bacteria or viruses within the living organism.

Studies in which these methods may be used include:

1. The dynamics of the antigen-antibody reaction.

2. Many tissues appear to participate in antibody production, the chief site depending on the mode of entry of the antigen which probably must first reach this site before antibody formation occurs. It appears that the lung is an important region of antibody formation.

3. Following intravenous injection of protein antigen in rabbits the normal decrease in antigen content of the blood was markedly accelerated by previous immunization and the rate of removal was further increased with heavily iodinated proteins.

4. Localization by radiochemical analysis shows that large amounts of intravenously injected antigens are found in lung, liver and spleen of immunized animals. More precise details are given by autoradiography; thus labelled antibody to kidney tissue as well as antibody serum injected into mice can be localized in specific parts of the glomeruli but mouse plasma antibodies could not be detected in the kidney, suggesting a close immunological relationship between lung and kidney tissues. These observations may be important to the study of autoimmunization.

5. The specific reaction of antibodies with particular tissues may be a possible means of inducing selective deposition of radioactive compounds in individual organs or localized sites; antigens appear to be less promising. The wide distribution of antibodies and antigens is a limitation to the technique and a present difficulty is the removal of antibodies which would combine with other than the selected tissue.

The value of this procedure in the study of skin reactions, kidney transplantation, allergies and contact dermatitis is also indicated.—*Raymond S. Quick, B.S.*

Clark, R. K., Brar, S. S., and Marinelli, L. D. Ionization of air by beta rays from point sources. *Radiology*, Jan., 1954, *64*, 94–104.

With the rapidly increasing use of radioisotopes in research, therapy, and radiation protection studies, the problem of accurately determining the distribution of energy imparted to chemical systems and to biological materials has greatly increased in importance. The problem requires: (a) evaluation of the dose as a function of the distance from a point source, and (b) integration at a given point of the energy contributed by beta particles originating within the range of the particles.

The authors have compiled valuable data regarding the ionization of air by beta rays from point sources. They studied the beta rays from four isotopes: P^{32}; Y^{91}; T^{204}; and RaE. The objective of their measurements was an accurate determination of the ionization distribution. The principal efforts were directed toward the demonstration that the observed ionization currents were due exclusively to the emitted particles progressing through the air and that all the effects due to solid scatterers or absorbers were properly accounted for.

The authors give a detailed description of their equipment and the procedures and technique used to measure electron effects in a low density material. Their results are given in extenso in the form of tables and graphs, which should be studied in the original article.—*A. W. Sommer, M.D.*

McGirr, E. M., and Hutchison, James H. The value of radioiodine (I^{131}) in juvenile myxoedema due to ectopic thyroid tissue. *Arch. Dis. Childhood*, Dec., 1954, *29*, 561–564.

The clinical features and radioactive isotope tracer findings in the instance of 2 children with ectopic thyroid tissue are presented.

One child, having had a thyroglossal duct cyst removed, became myxedematous. The other had not been operated upon but was found to have had thyroid tissue only in an aberrant location and was hypothyroid. Radioactive iodine tracer studies showed concentration of iodine in the region of the thyroglossal duct.

These studies show the value of radioactive iodine tracer studies in midline neck swellings and juvenile myxedema.—*Robert W. Emerick, M.D.*

Blumgart, Herrman L., Freedberg, A. Stone, and Kurland, George S. Treatment of incapacitated euthyroid cardiac patients with radioactive iodine; summary of results in treatment of 1,070 patients with angina pectoris or congestive failure. *J.A.M.A.*, Jan. 1, 1955, *157*, 1–4.

Several years previously the authors proposed the use of large doses of radioiodine to produce a hypothyroid state, as a palliative procedure for patients with angina pectoris and congestive failure not responding to routine therapeutic measures. The rationale is that the patient with decreased thyroid function has lessened circulatory requirements, which may be satisfied by even a diminished cardiac reserve.

Doses of 10–20 millicuries of I^{131} are given at weekly intervals for three weeks, followed by repeated doses at intervals of one to two months until hypothyroidism is achieved. Administration of larger single doses is discouraged because of the possibility of sudden release of hormone two to three weeks later, with temporary hyperthyroidism. Severe myxedema is controlled by oral thyroid, titrated when possible to result in minimal discomfort from each the cardiac disability and the hypothyroidism.

Therapeutic response in 983 patients from 49 cooperating clinics, and in 87 from the Beth Israel Hospital, was similar between the two groups. For angina pectoris, the treatment resulted in marked improvement for about 40 per cent of the patients, and good response in another 35 per cent. Marked improvement was noted in about 20 per cent of patients with congestive failure, and good response in about 38 per cent.

The authors emphasize that the treatment does not alter the basic disease processes, but adds a further useful treatment which may offer much comfort and activity to the patient with heart disease who has not been helped by other accepted therapeutic measures.—*R. Kenneth Loeffler, M.D.*

Kepp, R. K., Hartl, H., and Müller, K. Die Bedeutung von Radiogold 198 für die gynäkologische Strahlentherapie. (The significance of radiogold 198 for gynecological radiation therapy.) *Deutsche med. Wchnschr.*, Jan. 7, 1955, *80*, 19–21.

Of the radioactive isotopes which are suitable for the treatment of malignant tumors, radioactive gold (Au^{198}) due to its physical properties offers especially favorable possibilities. Since the half-life is 2.69 days its activity after ten days is below 10 per cent and after eighteen days below 1 per cent. It emits a mixed radiation composed of about 95 per cent of beta rays of max. 0.96 mev. and of 5 per cent of gamma rays of 0.411 mev.

On intracavitary application the surface effect, is predominant. On intratumoral application a high concentration of the dose in a small area is attained, and there is a very fast decrease of the dose toward the periphery.

The application of the radiogold is theoretically possible in three ways: (1) intravenously, when the radiogold is stored mostly in the reticuloendothelial system as of liver, spleen and bone marrow; (2) intracavitarily into peritoneal, pleural or pericardial cavities, which affords the chance of influencing preferably small nodules of the serosa; (3) intratumorally as into the carcinomatous cervix, into the parametria or into lymph node metastases. The two latter methods are applicable in gynecology.

The authors report 31 cases of intraperitoneal application of radioactive gold treated during the last 2½ years. Of 21 women with peritoneal and ovarian carcinosis treated with colloidal radiogold, 8 were dead within nine months. In 2 cases the therapy was started only recently. Eleven women are still living after one to two years and show definite improvement. Considering the very poor general condition, the palliative improvement was considerable. Only in 2 of 6 cases of ascites was a favorable effect of the radiogold observed. Side effects were minimal: twice a mild leukopenia, once an intestinal reaction with diarrhea and vomiting, once an agranulocytosis with a drop of leukocytes to 1,200 on the first, and 700 on the sixth day after the radiogold injection.

In discussing the intratumoral application, the authors state that they do not have any experience with radiogold therapy of the parametria. They used radiogold, however for lymph node metastases in carcinoma of the vulva and urethra. They treated 10 patients, 1 with supraclavicular metastases of an ovarian carcinoma, 3 with metastatic tumor infiltrates from primary carcinoma of the cervix and vagina and 6 with inguinal metastases from primary carcinoma of the vulva and urethra. Usually the skin over the injected area showed a strong erosive reaction after two to three weeks. At the same time a necrotic breakdown of the tumor with perforation and secretion of a purulent material was seen. After three to four weeks there was healing of the process with formation of a strong scar tissue. In 10 women treated intratumorally the tumor infiltration disappeared within a few weeks after the radiogold injection but metastases to other regions of the body occurred shortly thereafter, and most of the patients died in a short period.

In conclusion, there was a good palliative result of the intraperitoneal radiogold injection in 21 women with ovarian and peritoneal carcinosis. In 10 women treated intratumorally the injected portion of the tumor disappeared but there was no prevention of metastases to other parts of the body. The intratumoral treatment with radiogold proved to be the first effective method of healing inguinal lymph node metastases in carcinoma of the vulva and urethra where all other irradiation methods have failed so far. —*Hans Lewin, M.D.*

Ellis, Frank, and Oliver, R. Treatment of papilloma of bladder with radioactive colloidal gold Au^{198}. *Brit. M. J.*, Jan. 15, 1955, *1*, 136–139.

Villous papillomata of the bladder are usually multiple and there is abundant evidence to suggest

that many are premalignant in character. Some cases may be called "carcinoma in situ." The pathological distinction between benign and malignant papillomata may be impossible.

Treatment by cystoscopic fulguration, total or partial cystectomy, external roentgen therapy, radioactive solutions introduced in balloons, and centrally located solid radioactive sources has been described but each of these has certain drawbacks from the standpoint of recurrence after treatment, morbidity, mortality, and technical complexity. The authors decided to employ beta irradiation in the treatment of bladder papillomata, reasoning that the neoplasms would then be treated from all sides as they float freely in the solution. Only the epithelium of the normal structures would be irradiated to a very minimal depth due to the short range of the beta particles.

Radioactive colloidal gold was chosen as the most suitable material with a beta emission of 0.96 mev. Its colloidal nature would ensure relatively little absorption. The further advantage of being able to introduce the material via a catheter without performing a cystotomy was considered. It was estimated that about 300 mc. in 100 cc. of saline, if retained for two to three hours, allowing for dilution by the excreted urine, would deliver a dose of about 3,000 r to the bladder epithelium. Possible dangers anticipated were: (1) absorption into the blood stream or lymphatic channels of as little as 5–10 per cent of such a dose might have serious effects, and (2) if the material adhered to the bladder wall, huge doses might result (about 1,000,000 r/1 mc./cm.^{2} would be possible). This phenomenon was previously observed with thorium X. Careful tests showed that precipitation, adherence, or absorption did not occur in more than very small quantities. Accordingly, a patient with hematuria resulting from myriads of papillomata covering the entire bladder surface was treated by instilling 300 mc. Au^{198} in 100 cc. saline via a Foley catheter. This was left in place for 2½ hours, taking the necessary precautions to prevent leakage and the fluid was then drained, washing the bladder eight times until the return was colorless. Measurements immediately after and about twenty-four hours later, revealed less than 0.5 per cent of the Au^{198} to be retained in the bladder. No activity was detected elsewhere in the body. It was estimated that the dose to the bladder epithelium was 3,000 r, (2,700 rep beta dose, and 300 r gamma dose). This treatment was repeated in two months delivering a dose of 2,400 r to the bladder wall. Six weeks later the only residual papillomata were in a ring about the internal urethral meatus where the Foley bag prevented contact of the solution with the mucosa. These were treated locally with Co^{60} arranged in a Foley balloon with a dose of 3,000 r at a source-epithelium distance of 1 cm. The patient is now well and symptom-free fifteen months after the last treatment.

A suggested step-by-step routine for carrying out this method of treatment is described by the authors.

Multiple villous papillomatosis is ideally suited for treatment by this method. Papillomatosis with carcinoma may also be amenable and this type of treatment may be employed preliminarily to slow the surface activity of a lesion later to be implanted by radium, radon or radioactive tantalum or where a partial cystectomy is intended. The possibility of treating similar conditions of the kidney pelvis is suggested.

A nomogram is given for calculating the surface dose rate in the bladder and the method of dosage estimation is described in an appendix to the article. —*K. L. Krabbenhoft, M.D.*

Hinman, Frank, Jr., Miller, Gerald M., Smith, Gilbert I., James, Joseph, Ng, Elmer, and Sheline, Glen. The experimental background for retroperitoneal lymph node irradiation by radioactive colloids. *Surg., Gynec. & Obst.*, March, 1955, *100*, 345–350. (From: Departments of Surgery-Urology, and Radiology, University of California School of Medicine, San Francisco, Calif.)

The authors note that testicular tumors metastasize to the retroperitoneal lymph nodes, and that at present, surgery and deep roentgen therapy are used for treatment. However, they have conceived a third approach: irradiation of the retroperitoneal lymph nodes by radioactive colloids introduced by way of the presacral space.

Preparatory to human usuage, several animal experiments were performed. It was shown that particle size has an influence on distribution; small particles seemed to be rapidly cleared and more thoroughly distributed. The half-life of an isotope is also of importance. Gold has a relatively short half-life—2.7 days. Since chromic phosphate has a half-life of 14.3 days, a longer time for pick-up is available before decay renders it ineffective.

Radioactive colloidal gold, 15.755 millicuries in 43 cubic centimeters of saline, was injected into the presacral space of a 7 kilogram female dog. Approximately 20 per cent was excreted in the urine and feces. On the thirty-ninth day, autopsy showed no adverse radiation effect grossly. The right iliac lymph nodes were thickened and enlarged, with microscopic demonstration of fibrosis. Sections of rectum and ureters showed no evidence of injury.

Radioactive chromic phosphate was injected similarly into a male dog. Autopsy at sixty-three days after injection again showed lack of fibrosis around ureters or rectum. The lower iliac lymph nodes contained large amounts of radioisotope, with moderate amounts in the pre-aortic lymph nodes, and relatively little throughout the rest of the body except for the spleen. Since this animal had pain in

the left hind leg on the fifteenth day, and later developed muscular atrophy in this extremity, the authors conclude that the application of this technique to human patients is limited until further experimental work is done.—*R. Kenneth Loeffler, M.D.*

Hultborn, K. A., Larsson, L.-G., and Ragnhult, I. A study of the lymph drainage of the lower limb with the use of colloidal radiogold (Au^{198}). *Acta radiol.*, Feb., 1955, *43*, 139–144. (From: Radiumhemmet, Department of Surgery and Institute of Radiophysics, Karolinska Sjukhuset, Stockholm, Sweden.)

A preliminary investigation is reported on 5 cases in which a tracer dose of colloidal radiogold was injected into different parts of the lower extremities and direct lymph drainage was demonstrated in vivo.

The drainage was found to be as follows: Case 1, injection into the deep subcutaneous tissues of the left calf with drainage demonstrated to the lymph nodes in the popliteal fossa, groin, and iliac fossa. Cases 2 and 4, injection into the superficial subcutaneous tissues of the left calf with drainage to the inguinal and iliac lymph nodes. Case 3, intracutaneous injection into the left lateral thigh with drainage to the inguinal and iliac lymph nodes. Case 5, intracutaneous injection into the left calf with drainage to the popliteal and iliac lymph nodes.

From a practical standpoint, it is noted that in all cases, drainage to the iliac lymph nodes was found. Further study should increase our knowledge of regional lymph node drainage and give additional indications for adequate treatment.—*George A. Miller, M.D.*

Talairach, J., Ruggiero, G., Aboulker, J., and David, M. A new method of treatment of inoperable brain tumours by stereotaxic implantation of radioactive gold—a preliminary report. *Brit. J. Radiol.*, Feb., 1955, *28*, 62–74. (From: Centre neurochirurgical de l'Hôpital Ste Anne, Paris, France.)

As a means of treating brain tumors which are either too extensive or critically situated to permit satisfactory surgical attack, the implantation of radioactive gold seeds is described.

After localization, and estimation of tumor size and nature by physical examination, roentgenographic techniques, and electroencephalography, the decision of operability is made. If it is considered that the lesion is inoperable, or that operation is attended by excessive mortality or morbidity, gold seeds are implanted. These are inserted through a burr hole with a 2 mm. diameter probe, the position controlled by stereotaxometry. Essentially, spatial relation is established in relation to a metal plate fixed on the skull.

Case histories are presented of 5 patients treated in this manner with one or several seeds of total activity of 40 to 60 millicuries. The response of 3 of these patients was very encouraging, and the other 2 cases were unharmed. It is anticipated that refinements in technique should result in further improvements in results.—*R. Kenneth Loeffler, M.D.*

Hultborn, K. A., and Jonsson, L. I. The use of colloidal Au^{198} for the detection of lymph nodes in radical excision of the breast. *Acta radiol.*, Feb., 1955, *43*, 132–138. (From: Radiumhemmet, Department of Surgery, Institute of Radiopathology and Institute of Radiophysics, Karolinska Sjukhuset, Stockholm, Sweden.)

A study by Monroe in 1948 suggested that the greater the number of lymph nodes removed in the operation specimen in carcinoma of the breast, the greater were the chances of freedom from recurrence. A similar report was made by Sprong and Pollock in 1951.

To assist in a more complete lymph node removal, the authors made subareolar injections of radioactive colloidal gold in 3 cases some days before radical excision. When the surgeon considered the axillary dissection complete, it was possible to detect with a sensitive directional scintillation counter, additional lymph nodes in 2 of the cases.—*George A. Miller, M.D.*

Osgood, Edwin E., Seaman, Arthur J., and Tivey, Harold, with the technical assistance of Moffat, Charlotte A., and Hughes, Margret E. Comparative survival times of x-ray treated versus P^{32} treated patients with chronic leukemias under the program of titrated, regularly spaced total-body irradiation. *Radiology*, March, 1955, *64*, 373–381. (Address: Dr. Osgood, 3181 S. W. Sam Jackson Park Road, Portland, Ore.)

The authors report the results of a study of the survival time of 163 patients with chronic leukemia treated in the period from January, 1941, to July, 1951. The patients studied included all who were referred for treatment, even those who were moribund at the time treatment was started. All patients were treated by the method of titrated, regularly spaced total body irradiation. The basic principles of treatment were identical for all these patients, but 23 received spray roentgen irradiation, and 140 were given internal irradiation by intravenously injected radioactive phosphorus (P^{32}).

The principles of treatment by the method of titrated, regularly spaced total body irradiation are:

(a) To bring the patient's disease under initial control by small doses (ca. 10 to 20 r or equivalent P^{32}) at intervals of one to two weeks.

(b) To maintain that control by minimal doses (10 to 20 r) at such appropriate regular intervals that the patient remains in an optimum state of health.

(c) To adjust the treatment to fit the needs of the individual, *i.e.*, to titrate the amount of irradiation given against the clinical condition. One must not treat the leukocyte, but the entire patient.

With the small doses used in this study, radiation acts primarily on leukemic cells by inhibiting mitosis in the granulocytic series, but it may be capable of killing lymphocytes, as well as interfering with their proliferation. The life span is approximately five days for cells of the granulocytic series and someting in excess of thirty days for the lymphocytes of chronic leukemia. It is considered desirable to follow chronic leukemia patients at intervals consistent with the short life span of these cells.

The prognosis for survival was not significantly different whether the total-body irradiation was delivered externally by the spray technic or internally from radioactive phosphorus. No radiation sickness was encountered with either type of therapy. The results of the regularly spaced, titrated, whole-body irradiation technique are superior to those for a series of cases of leukemia treated by conventional methods which were assembled from the literature.—*A. W. Sommer, M.D.*

Benua, Richard S., and Dobyns, Brown M. Iodinated compounds in the serum, disappearance of radioactive iodine from the thyroid, and clinical response in patients treated with radioactive iodine. *J. Clin. Endocrinol. & Metabol.*, Jan., 1955, *15*, 118–130.

Although most of the organically bound radioiodine in the blood after therapeutic doses of I^{131} is in the form of thyroxine, other compounds have been reported present. The question in point is whether any or all of these compounds (butanol-insoluble organic iodine, diiodotyrosine, monoiodotyrosine and triiodothyronine) are the result of irradiation of the thyroid gland.

Following radioactive iodine therapy in 31 patients, 26 with Graves' disease, 4 with cancer of the thyroid and 1 with a toxic nodular goiter, samples of blood were collected at frequent intervals, sometimes daily, and chromatographic fractionations of the serum were made. The chromatographic technique is discussed in detail. The authors point to the difficulty of differentiating between the results which represent radiation effects, those which represent disease processes and those which represent normal physiologic events. They believe this indirect evidence allows tentative interpretations.

Chromatography showed a decreased level of radioiodide in the serum in one to two days. This was thought to be due to clearance of the radioiodide from the blood. A secondary rise occurred after three to six days, due either to radiation effect or to deiodination of thyroxine.

Triiodothyronine was present in the serum of 19 of the patients shortly after receiving the therapeutic dose of I^{131}. This was highest in the patients with evidence of most severe thyrotoxicosis, and its rate of appearance and concentration could not be correlated with the amount and duration of irradiation of the thyroid gland. For these reasons it was considered that triiodothyronine is related to degree of thyrotoxicosis and not to radiation effect.

Monoiodotyrosine was found present in the serum of 14 patients. In 7 instances it was present on the first day after receiving the therapeutic dose of I^{131}. Some patients who received large amounts of I^{131} showed no evidence of this compound. Presence of this compound could not be related either to radiation effect or thyroid hyperfunction.

Diiodotyrosine was found present in the serum of 6 patients. These received the most radiation to the thyroid (by microcurie/estimated gram days). The authors feel that the presence of this compound is the result of irradiation of thyroid tissue.—*Robert W. Emerick, M.D.*

Richardson, Jasper E., and Brucer, Marshall. Modification of electron filter to improve light localization of a cobalt-60 beam. *Radiology*, March, 1955, *64*, 398–403. (Address: Dr. Brucer, Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tenn.)

The authors report the result of studies to determine the distribution of ionization in the first few millimeters of tissue-like material with a cobalt-60 teletherapy unit. When short cone-to-skin distances are used, it is advantageous to filter secondary electron emission from the collimating system with a thin sheet of cadmium over the cone, in order to minimize the skin dose.

A method was devised which permits use of the light localizer of the teletherapy unit without having to remove and replace the filter with each use. A lucite cap was constructed to fit over the end of the cone. The cadmium filter, 0.25 mm. thick, was attached to the lucite so as to cover the opening of the cone, except for a narrow slit (about 1 mm.) around the edges. With this arrangement, a band of light delineates the true geometrical beam of gamma rays and the width of the geometrical penumbra.—*A. W. Sommer, M.D.*

Miscellaneous

Attix, Frank H., and DeLa Vergne, LeRoy. Plate separation requirements for standard free-air ionization chambers. *Radiology*, Dec., 1954, *63*, 853–866.

A comparative study of free-air ionization cham-

bers for measuring roentgen-ray energies up to 250 kv. is discussed.

Details relative to construction of various types of ionization chambers are presented. Measurements of kev. electrons produced by a localized roentgen-ray beam in chambers designed with various distances of plate separation, variations of height, and varying lengths of irradiated air columns were made.

The study demonstrated that the present standard chambers of the National Bureau of Standards and of the National Physical Laboratory record less ionization than actually takes place. Although Kemp and Hall designed a larger free-air chamber with greater accuracy, the present study indicates need for even larger size and different design.

It is concluded that the field-distortion problem is more serious than has been heretofore supposed, and new criteria must be established for designing distortion-free chambers. A detailed description of such a chamber will be the subject of a later paper.—*E. E. Seedorf, M.D.*

Rushmer, Robert, F., Ellis, Richard M., and Nash, Alden A. Stereo-cinefluorography; motion roentgenography in three dimensions. *Radiology*, Feb., 1955, *64*, 191–196.

In order to broaden the application of roentgenographic studies of internal organs, a technique for three-dimensional visualization of cinefluorographic films has been developed by the authors. There are two important visual clues to three dimensional orientation in visualizing roentgenographic images: (1) Given two objects, traveling at the same rate, the one which is closer to the observer appears to move faster. During rotation around an axis, points on the near side move in one direction and those on the far side move in the other. This is standard procedure during fluoroscopy. (2) The eyes are separated by a slight distance so that slightly different images fall on the two retinas. This is referred to as binocular parallax. This principle is exploited by using two cameras to represent the eyes.

Stereoscopic cinefluorography of both moving and stationary subjects can be obtained by mounting two roentgen tubes side by side. The images formed on the underlying fluorescent screen will be dissimilar To avoid diplopia, as would occur if the two tubes were fired simultanelusly, a triggering mechanism is required to fire the tubes alternately and to expose frames on the film to the alternating images. The mechanics of this device as well as the equipment required are described in detail.

The cinefluorographic exposures are made on 35 mm. film to facilitate frame-by-frame analysis. Since it is inconvenient to project film of this dimension, all projection prints are routinely reduced to 16 mm. film. The authors describe a simple reduction printer of their device for accomplishing this. Projection of the stereo-cinefluorographic films is satisfactorily obtained by means of a polarization device which is fully described. The images must be projected on flat aluminum screens and viewed with standard polarized glasses.

The ultimate usefulness and limitations of the method have not been fully established. The most striking three-dimensional impressions have been obtained of structures and objects with a high degree of radiopacity and relatively clear-cut margins, such as bones and joints, bronchograms, gastrointestinal studies with barium, and opaque vascular studies. An annoying flicker is produced when large areas of the screen are illuminated during projection. A technique of split-frame reduction printing is being developed to overcome this. Several other limitations, such as sharpness of images due to geometrical arrangement of the objects studied, poor definition of objects of similar density, and eye strain, are encountered. These problems are under study at the present time.—*Michael J. Healy, M.D.*

Biel, Leonard, Jr., and Eliasoph, James L. A technique for retrorectal gas insufflation. *J. Urol.*, Dec., 1954, *72*, 1255–1259.

The injection of non-opaque gas contrast medium into the retroperitoneal space for diagnostic purposes was first undertaken by Carelli in 1921, and was popularized by Cahill in 1935. Ruiz Rivas, in 1950, advised the use of the retrorectal or presacral site for injection as eliminating many of the undesirable features of perirenal insufflation. Together with the simultaneous use of intravenous or retrograde pyelography and laminagraphy, presacral injection of air has been shown to be relatively safe and of value in the demonstration of the kidneys, adrenals, liver and spleen, etc.

In this article, the authors present a simple modification of the technique of retrorectal insufflation which has resulted in increased ease of performance, shortening of the time of injection and increased comfort for the patient and operator.

After suitable skin preparation of the perianal area and the administration of a cleansing enema, the patient is placed in the knee-chest position. With one finger in the rectum to guide the positioning of the needle, an 18 or 20 gauge, 3 inch, short bevel, spinal needle fitted with an obturator is inserted with the tip in the midline, opposite the lower sacral segments. The obturator is removed and the needle is then connected with a three-way stopcock, a 50 cc. syringe is attached to one limb of the stopcock and a standard pneumothorax gas measuring device filled with oxygen is attached to the third limb. Oxygen is drawn into the syringe and injected through the needle into the presacral region. Considerable pressure is often required for the first 100–200 cc., but following this, the tissue planes appear to open up and practically no resistance is felt to further gas

injection. A total of 1,250–1,750 cc. of oxygen is administered for adult patients, depending upon their size. The patients may complain of mild transitory abdominal cramps. Some degree of mediastinal emphysema will develop in all patients and crepitus may be palpated in the tissues of the neck. This is not a serious complication.

The authors have used this technique in more than 100 instances without noting any embolic phenomenon or other accidents.—*George W. Chamberlin, M.D.*

Cole, L. J., Fishler, M. C., and Ellis, M. E. Studies on the nature of the radiation protection factor in mouse spleen. *Radiology*, Feb., 1955, *64*, 201–209.

In previous publications the authors had demonstrated that a splenic substance injected into post-irradiated mice, that had received a lethal dose of irradiation, greatly increased their survival rate as compared to 100 per cent mortality of the mice which did not receive the splenic substance. They had demonstrated that the substance was associated with the nuclei fraction of the spleen and further that the factor is noncellular in nature and that it is a desoxyribonucleoprotein.

The present article reports additional experimental studies designed to obtain further insight into the nature of the spleen factor.

The following tentative conclusions appear to be the properties of the radiation protection factors in the spleen of young LA f 1 mice; the factor appears to be a non-dialyzable, unstable, heat-labile, radiosensitive substance associated with the nuclear fraction. Its susceptibility to the action of desoxyribonuclease and trypsin and its resistance to ribonuclease are what would be expected if the substance were a DNA-protein complex. The factor appears to be specific in origin: it is found in mouse spleen, and probably in bone marrow, but is apparently not elaborated by thymus tissue, nor by liver, muscle, or lung tissue.

It is emphasized that these are only tentative conclusions based on experimental data available at this time.—*E. E. Seedorf, M.D.*

Schlumberger, Hans, G., and Vazquez, Jacinto J. Pathology of total body irradiation in the monkey. *Am. J. Path.*, Dec., 1954, *30*, 1013–1047.

Ninety-two rhesus monkeys were given total body roentgen irradiation in amounts varying from 300 to 900 r to determine the lethal dose for 50 per cent in thirty days (LD 50/30). This amount was found to be approximately 550 r.

The lesions encountered in the animals corresponded closely to the gross and microscopic findings in man. The hematopoietic system showed the earliest and most constant sign of destruction of the blood forming elements of the marrow and loss of lymphocytes from the lymph nodes and spleen.

Petechiae were observed in the skin, lungs, epicardium, stomach and colon.

Necrotic gingivitis and stomal ulceration similar to that seen in humans was found in a significant number of animals receiving over 300 r and surviving over two weeks.

No significant changes were observed in the central nervous system, kidneys, liver or musculoskeletal system.—*S. G. Belote, M.D.*

Ellinger, Friedrich, Morgan, Jasper, E., and Cook, Elsworth B. Reproducibility of the lethal effect of total-body irradiation in mice. *Radiology*, Feb., 1955, *64*, 210–218.

A systematic investigation of the effects of total body irradiation on a variety of small laboratory animals has been carried on by the authors during the past fifteen years. A positive relationship between increase of the administered roentgen-ray dose and the percentage mortality has been demonstrated by these studies. The lethal effects of this total body irradiation upon fish or mammals can be used advantageously for the study of numerous problems in medical radiation biology such as depth dose determination, the influence of dose fractionation, and the pharmacological analysis of the acute radiation syndrome.

Of great importance in studying this effect is the reproducibility of this effect over a period of time and with many different groups of the animals being used. Certain procedural points essential to optimum reproducibility are:

A. Physical
   (1) Stability of line voltage.
   (2) Stability of dose determination.
   (3) Stability of field characteristics.
   (4) Consistency of backscatter.

B. Biological
   (1) Insurance of optimal health of animals by
      (a) Quarantine of at least 2 weeks prior to irradiation.
      (b) Weight control.
   (2) Use of only one sex (preferably males).
   (3) Individual caging of animals.
   (4) Meticulous after-care of irradiated animals by
      (a) Change of cages at least once a week.
      (b) Reduction of air contamination.
      (c) Temperature control of animal room.

With the above conditions being followed, it was possible to reproduce over a period of several years the lethal effect in mice by a stated roentgen-ray dose given as total body irradiation. By using sufficiently large number of animals, very reliable data on the biological effects of roentgen-ray doses differing by ± 2.5 per cent were obtained.—*D. N. Dysart, M.D.*